Related case 09/738879.


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=> fil reg
FILE 'REGISTRY' ENTERED AT 14:46:04 ON 07 DEC 2002
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STRUCTURE FILE UPDATES:    6 DEC 2002  HIGHEST RN 475385-56-9
DICTIONARY FILE UPDATES:   6 DEC 2002  HIGHEST RN 475385-56-9

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available.  See HELP
PROPERTIES for more information.  See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> d sta que l21
L18                 STR
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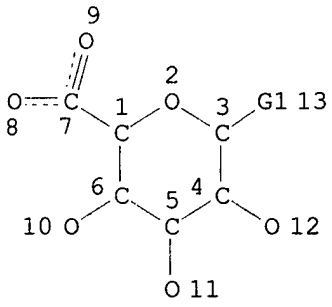
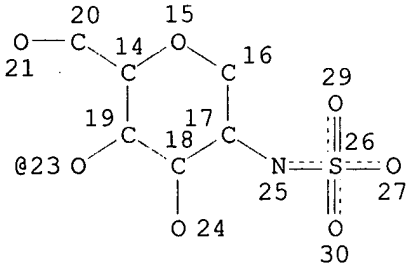
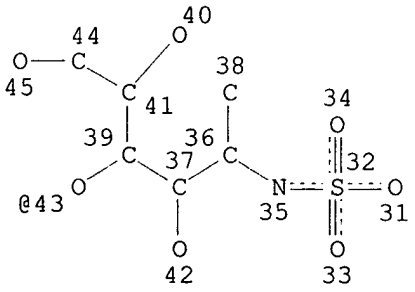
Jan Delaval
Reference Librarian
Biotechnology & Chemical Library
CM1 1E07 – 703-308-4498
jan.delaval@uspto.gov





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VAR G1=23/43
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  43

STEREO ATTRIBUTES: NONE
L21          373 SEA FILE=REGISTRY SSS FUL L18
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100.0% PROCESSED 494 ITERATIONS 373 ANSWERS
SEARCH TIME: 00.00.01

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               SET COST OFF

     FILE 'REGISTRY' ENTERED AT 13:58:07 ON 07 DEC 2002
               E K5/CN
L1             1 S E4

     FILE 'HCAPLUS' ENTERED AT 13:58:49 ON 07 DEC 2002
               E ORESTE P/AU
L2            32 S E3-E5
               E ZOPPETTI G/AU
L3            46 S E3,E4
L4            23 S L2 AND L3
L5            13 S L2,L3 AND K5(L)?SACCHARID?
               E IT2000-MI665/AP,PRN
L6             2 S E3,E4
L7             2 S L6 AND L2-L6
L8            11 S L5 NOT L7
L9            13 S L2,L3 AND CARBOHYDRATE?/SC,SX,CW
L10            5 S L9 NOT L5-L8
               SEL DN AN 2 5
L11            2 S L10 AND E1-E6
L12           15 S L7,L8,L11 AND L2-L11
               SEL RN

     FILE 'REGISTRY' ENTERED AT 14:03:17 ON 07 DEC 2002
L13           54 S E7-E60
L14            8 S L13 AND OC5/ES
L15           10 S L13 AND (N AND S)/ELS
L16            6 S L15 AND L14
L17            6 S L14,L15 NOT L16
L18              STR
L19           11 S L18
               E K 5/CN
L20            1 S E11
L21          373 S L18 FUL
               SAV L21 KRISH950/A

     FILE 'HCAPLUS' ENTERED AT 14:09:25 ON 07 DEC 2002
L22            7 S L20
L23          129 S (K5 OR K 5)(L)?SACCHARID?
L24          129 S L22,L23
L25          279 S L21
L26            3 S L24 AND L25
L27           13 S L2,L3 AND L24
L28            2 S L2,L3 AND L25
L29            3 S L26,L28
L30            5 S L7,L29
L31           16 S L12,L26-L30
L32            3 S L25 AND L31
L33           16 S L31,L32

     FILE 'REGISTRY' ENTERED AT 14:15:08 ON 07 DEC 2002
L34         1043 S ?EPIMERASE?/CNS

     FILE 'HCAPLUS' ENTERED AT 14:15:20 ON 07 DEC 2002
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L35        1984 S L34
L36        2049 S ?EPIMERASE?
L37        2585 S L35,L36
L38           9 S L37 AND L24
L39           1 S L37 AND L25
L40          22 S L33,L38,L39
L41       11238 S ?EPIMERI?
L42          13 S L41 AND L24
L43           1 S L41 AND L25
L44          27 S L40,L42,L43
L45           0 S L44 AND EPIMERIS?
L46          13 S L44 AND EPIMERIZ?
L47          27 S L44,L46
L48          43 S L24,L25 AND (GLUCURON? AND IDURON?)

     FILE 'REGISTRY' ENTERED AT 14:19:38 ON 07 DEC 2002
L49           1 S DIMETHYL SULFOXIDE/CN
L50           1 S METHANOL/CN
                E BARIUM, ION/CN
L51           1 S E19
                E CALCIUM, ION/CN
L52           1 S E23
                E MAGNESIUM, ION/CN
L53           1 S E17
                E MANGANESE, ION/CN
L54           1 S E20
                E BARIUM CHLORIDE/CN
L55           1 S E3
                E CALCIUM CHLORIDE/CN
L56           1 S E3
                E MAGNESIUM CHLORIDE/CN
L57           1 S E3
                E MANGANESE CHLORIDE/CN
L58           2 S E3
                E PYRIDINE SULFUR TRIOXIDE/CN
L59           1 S E3
                E TRIMETHYLAMINE SULFUR TRIOXIDE/CN
L60           1 S E3
L61           1 S E4
                E SODIUM BOROHYDRIDE/CN
L62           1 S E3
L63          46 S L13 NOT OC5/ES
L64          23 S L63 NOT UNSPECIFIED
L65          12 S L64 NOT L49-L62
L66           1 S L65 AND NITROUS ACID/CN
L67           2 S L65 AND NC5/ES
L68           3 S L65 AND O3S
L69           7 S L65 NOT L66-L68

     FILE 'HCAPLUS' ENTERED AT 14:28:08 ON 07 DEC 2002
L70       52343 S L49 OR DMSO OR DIMETHYLSULFOXIDE OR DIMETHYLSULPHOXIDE OR (DI
L71      419479 S L50 OR MEOH OR METHANOL OR METHYLALCOHOL OR METHYL ALCOHOL
L72           1 S L24,L25 AND L70 AND L71
L73           2 S L24,L25 AND L51-L58
L74          16 S L24,L25 AND (DIVALENT(L)CATION OR BARIUM OR CALCIUM OR MAGNES
L75           1 S L24,L25 AND (L62 OR (NA OR SODIUM)()BOROHYDRIDE)
L76           8 S L24,L25 AND L59-L61,L66-L68
L77          43 S L72-L76,L47
L78           8 S L48 AND L77
L79          30 S L72,L73,L75,L76,L78,L47
L80          23 S L24,L25 AND SULFAT?/CW
L81           7 S L24,L25 AND DEACET?/CW
L82          13 S L79 AND L80,L81
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L83          40 S L79-L82
L84          14 S L83 AND ?GLYCOSAMINOGLYCAN?
L85          27 S L83 AND L24
L86          27 S L83 AND L47
L87           5 S L83 NOT L84-L86
L88        4995 S ANTITHROMBIN III
L89        4475 S FACTOR XA
L90        5715 S FACTOR II

     FILE 'REGISTRY' ENTERED AT 14:37:49 ON 07 DEC 2002
L91           3 S 9000-94-6 OR 9002-04-4 OR 9002-05-5
                E FACTOR II/CN
L92           1 S E3 NOT CO/ELS

     FILE 'HCAPLUS' ENTERED AT 14:38:59 ON 07 DEC 2002
L93       22987 S L91,L92
L94           9 S L83 AND L88-L90,L93
L95          28 S L86,L94
L96          12 S L83 NOT L95
L97          40 S L2,L3 NOT L95,L96
                SEL DN AN 1
L98           1 S L97 AND E1-E3
L99          29 S L98,L95 AND L2-L12,L22-L33,L35-L48,L70-L90,L93-L98
L100         12 S L83 NOT L99
                SEL DN AN 3 5
L101          2 S L100 AND E4-E9
L102         31 S L99,L101
                SEL HIT RN

     FILE 'REGISTRY' ENTERED AT 14:44:29 ON 07 DEC 2002
L103         48 S E10-E57
L104         25 S L103 AND L21
L105         23 S L103 NOT L104
L106          1 S L105 AND K 5
L107         22 S L105 NOT L106

     FILE 'REGISTRY' ENTERED AT 14:46:04 ON 07 DEC 2002

=> d ide can l106

L106 ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2002 ACS
RN   42615-44-1  REGISTRY
CN   K 5 (polysaccharide) (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   K 5
MF   Unspecified
CI   PMS, MAN
PCT  Manual registration
LC   STN Files:   BIOSIS, CA, CANCERLIT, CAPLUS, MEDLINE, TOXCENTER, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
               7 REFERENCES IN FILE CA (1962 TO DATE)
               1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
               7 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE   1:  136:380105

REFERENCE   2:  136:167613

REFERENCE   3:  135:267246

REFERENCE   4:  132:46781
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REFERENCE 5: 129:3741

REFERENCE 6: 118:55633

REFERENCE 7: 79:53691

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FILE 'HCAPLUS' ENTERED AT 14:46:34 ON 07 DEC 2002
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FILE COVERS 1907 - 7 Dec 2002 VOL 137 ISS 24
FILE LAST UPDATED: 6 Dec 2002 (20021206/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

=> d all hitstr tot l102

L102 ANSWER 1 OF 31 HCAPLUS COPYRIGHT 2002 ACS
AN **2002:813944** HCAPLUS
DN **137:304779**
TI Use of sulfated bacterial polysaccharides suitable for the inhibition of angiogenesis
IN **Zoppetti, Giorgio; Oreste, Pasqua Anna**; Presta, Marco
PA Universita Degli Studi Di Brescia, Italy
SO PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-737
ICS A61P029-00; A61P035-00; A61P017-06
CC 1-8 (Pharmacology)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002083155	A1	20021024	WO 2002-IB1138	20020410

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,

CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRAI IT 2001-MI779 A 20010412
AB The present invention refers to the use of N,O-sulfated K5 having a degree of sulfation of at least 2, and of their pharmaceutical acceptable salts for the prepn. of medicaments for treating angiogenesis-dependent diseases.
ST angiogenesis inhibition sulfated bacterial polysaccharide
IT Proteoglycans, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(heparitin sulfate-contg., ternary complex; use of sulfated bacterial polysaccharides suitable for the inhibition of angiogenesis)
IT Polysaccharides, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sulfated; use of sulfated bacterial polysaccharides suitable for the inhibition of angiogenesis)
IT Fibroblast growth factor receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type 1, ternary complex; use of sulfated bacterial polysaccharides suitable for the inhibition of angiogenesis)
IT Angiogenesis inhibitors
Anticoagulants
Escherichia coli
(use of sulfated bacterial polysaccharides suitable for the inhibition of angiogenesis)
IT 106096-93-9D, Fibroblast growth factor 2, ternary complex
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(use of sulfated bacterial polysaccharides suitable for the inhibition of angiogenesis)
RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Casu, B; CARBOHYDRATE RESEARCH 1994, V263(2), P271 HCAPLUS
(2) Cipolletti, G; WO 9834958 A 1998 HCAPLUS
(3) Folkman, J; ADVANCES IN EXPERIMENTAL MEDICINE AND BIOLOGY 1992, V313, P355 HCAPLUS
(4) Hahnenberger, R; GLYCOBIOLOGY 1993, V3(6), P567 HCAPLUS
(5) Kasbauer, C; CARBOHYDRATE RESEARCH 2001, V330(3), P427 HCAPLUS
(6) Leali, D; JOURNAL OF BIOLOGICAL CHEMISTRY 2001, V41(276), P37900
(7) Torri, G; WO 9809636 A 1998 HCAPLUS
(8) Tubby, D; WO 9217507 A 1992 HCAPLUS

L102 ANSWER 2 OF 31 HCAPLUS COPYRIGHT 2002 ACS
AN 2002:676062 HCAPLUS
DN 137:200359
TI Highly sulfated derivatives of **k5 polysaccharide** and their preparation
IN **Zoppetti, Giorgio; Oreste, Pasqua Anna**
PA Italy
SO PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C08B037-00
ICS A61K031-715
CC 16-4 (Fermentation and Bioindustrial Chemistry)
Section cross-reference(s): **44**
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002068477	A1	20020906	WO 2002-IB561	20020226

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GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI IT 2001-MI397 A 20010227

AB The purifn. of the Escherichia coli **K5 polysaccharide** by treatment with iso-Pr alc. and elimination of lipophilic substances is described. The purified product can be used to prep., after N-deacetylation, new N,O-sulfated **polysaccharides** with high degree of sulfation.

ST polysaccharide sulfation

IT Escherichia coli
Sulfation
(highly sulfated derivs. of **k5 polysaccharide** and their prepn.)

IT **Polysaccharides**, preparation
RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); PUR (Purification or recovery); RCT (Reactant); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(highly sulfated derivs. of **k5 polysaccharide** and their prepn.)

IT **3162-58-1**, Trimethylamine sulfur trioxide **26412-87-3**, Pyridine sulfur trioxide
RL: RCT (Reactant); RACT (Reactant or reagent)
(highly sulfated derivs. of **k5 polysaccharide** and their prepn.)

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE
(1) Inalco; WO 9834958 A 1998 HCAPLUS
(2) Inalco; WO 9842754 A 1998 HCAPLUS
(3) Inalco; WO 0102597 A 2001 HCAPLUS
(4) Italfarmaco S P A; WO 9217507 A 1992 HCAPLUS
(5) Manzoni, M; JOURNAL OF BIOACTIVE AND COMPATIBLE POLYMERS 1993, V8(3), P251 HCAPLUS

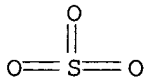
IT **3162-58-1**, Trimethylamine sulfur trioxide **26412-87-3**, Pyridine sulfur trioxide
RL: RCT (Reactant); RACT (Reactant or reagent)
(highly sulfated derivs. of **k5 polysaccharide** and their prepn.)

RN 3162-58-1 HCAPLUS

CN Methanamine, N,N-dimethyl-, compd. with sulfur trioxide (1:1) (9CI) (CA INDEX NAME)

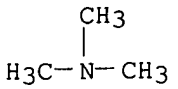
CM 1

CRN 7446-11-9
CMF O3 S



CM 2

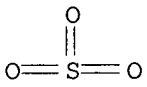
CRN 75-50-3
CMF C3 H9 N



RN 26412-87-3 HCAPLUS
CN Sulfur trioxide, compd. with pyridine (1:1) (9CI) (CA INDEX NAME)

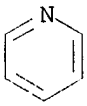
CM 1

CRN 7446-11-9
CMF O3 S



CM 2

CRN 110-86-1
CMF C5 H5 N



L102 ANSWER 3 OF 31 HCAPLUS COPYRIGHT 2002 ACS
AN 2002:392262 HCAPLUS
DN 136:380105
TI **Glycosaminoglycans** derived from **k5** **polysaccharide** having high anticoagulant and antithrombotic activities and process for their preparation
IN **Oreste, Pasqua; Zoppetti, Giorgio**
PA Italy
SO U.S. Pat. Appl. Publ., 39 pp., Cont.-in-part of U.S. Ser. No. 738,879.
CODEN: USXXCO
DT Patent
LA English
IC ICM C12P019-04
ICS C08B037-00
NCL 536054000
CC 1-8 (Pharmacology)
Section cross-reference(s): **33**
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002062019	A1	20020523	US 2001-950003	20010912 <--
	IT 2000MI0665	A1	20011001	IT 2000-MI665	20000330 <--
	WO 2002050125	A2	20020627	WO 2001-IB2492	20011217
	WO 2002050125	A3	20020822		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,

PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2002022358 A5 20020701 AU 2002-22358 20011217
PRAI IT 2000-MI665 A 20000330 <--
US 2000-738879 A2 20001218
US 2001-950003 A 20010912
WO 2001-IB2492 W 20011217

AB **Glycosaminoglycans** derived from **K5** **polysaccharide** having high anticoagulant and antithrombotic activity and useful for the control of coagulation and as antithrombotic agents are obtained starting from an optionally purified **K5** **polysaccharide** by a process comprising the steps of N-deacetylation/N-sulfation, C5 **epimerization**, O-oversulfation, selective O-desulfation, 6-O-sulfation, N-sulfation, and optional depolymn., in which said **epimerization** is performed with the use of the enzyme glucoronosyl C5 **epimerase** in soln. or in immobilized form in the presence of **divalent cations**. New, particularly interesting antithrombin compds. are obtained by controlling the reaction time in the selective O-desulfation step and submitting the product obtained at the end of the final N-sulfation step to depolymerizazion.

ST **glycosaminoglycan k5 polysaccharide** deriv anticoagulant antithrombotic

IT Liver
(bovine, glucuronosyl C-5 **epimerase** of; **glycosaminoglycans** derived from **k5** **polysaccharide** having high anticoagulant and antithrombotic activities and process for their prepn.)

IT **Cations**
(**divalent; glycosaminoglycans** derived from **k5 polysaccharide** having high anticoagulant and antithrombotic activities and process for their prepn.)

IT Immobilization, molecular
(enzyme, of glucuronosyl C-5 **epimerase**; **glycosaminoglycans** derived from **k5** **polysaccharide** having high anticoagulant and antithrombotic activities and process for their prepn.)

IT Anticoagulants
Deacetylation
Drugs
Epimerization
Sulfation
(**glycosaminoglycans** derived from **k5** **polysaccharide** having high anticoagulant and antithrombotic activities and process for their prepn.)

IT Alkaline earth salts
Salts, preparation
RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(**glycosaminoglycans** derived from **k5** **polysaccharide** having high anticoagulant and antithrombotic activities and process for their prepn.)

IT **Glycosaminoglycans**, biological studies
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**glycosaminoglycans** derived from **k5** **polysaccharide** having high anticoagulant and antithrombotic activities and process for their prepn.)

IT Quaternary ammonium compounds, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(**glycosaminoglycans** derived from **k5** **polysaccharide** having high anticoagulant and antithrombotic activities and process for their prepn.)

IT Escherichia coli
(**k5 polysaccharides** from; **glycosaminoglycans** derived from **k5** **polysaccharide** having high anticoagulant and antithrombotic activities and process for their prepn.)

IT Mast cell
(mastocytoma, murine, glucuronosyl C-5 **epimerase** of; **glycosaminoglycans** derived from **k5** **polysaccharide** having high anticoagulant and antithrombotic activities and process for their prepn.)

IT **Sulfation**
(retrosulfation; **glycosaminoglycans** derived from **k5** **polysaccharide** having high anticoagulant and antithrombotic activities and process for their prepn.)

IT **9000-94-6, Antithrombin III**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(binding to; **glycosaminoglycans** derived from **k5** **polysaccharide** having high anticoagulant and antithrombotic activities and process for their prepn.)

IT **7782-77-6**, Nitrous acid
RL: RCT (Reactant); RACT (Reactant or reagent)
(degrdn. with; **glycosaminoglycans** derived from **k5** **polysaccharide** having high anticoagulant and antithrombotic activities and process for their prepn.)

IT **112567-86-9**, Heparin precursor glucuronate 5-**epimerase**
RL: BCP (Biochemical process); CAT (Catalyst use); BIOL (Biological study); PROC (Process); USES (Uses)
(**glycosaminoglycans** derived from **k5** **polysaccharide** having high anticoagulant and antithrombotic activities and process for their prepn.)

IT **7773-01-5, Manganese chloride (MnCl2)** **7786-30-3, Magnesium chloride (MgCl2)**, uses **10043-52-4, Calcium chloride (CaCl2)**, uses **10361-37-2, Barium chloride (BaCl2)**, uses **14127-61-8, Calcium(2+)**, uses **16397-91-4, Manganese(2+)**, uses **22537-22-0, Magnesium(2+)**, uses **22541-12-4, Barium(2+)**, uses
RL: NUU (Other use, unclassified); USES (Uses)
(**glycosaminoglycans** derived from **k5** **polysaccharide** having high anticoagulant and antithrombotic activities and process for their prepn.)

IT 2052-49-5, Tetrabutylammonium hydroxide **16940-66-2, Sodium borohydride** **26412-87-3**, Pyridine sulfur trioxide **42615-44-1, k5 Polysaccharide**
RL: RCT (Reactant); RACT (Reactant or reagent)
(**glycosaminoglycans** derived from **k5** **polysaccharide** having high anticoagulant and antithrombotic activities and process for their prepn.)

IT 9012-36-6D, Sepharose 4b, CNBr activated
RL: BUU (Biological use, unclassified); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(immobilization carrier; **glycosaminoglycans** derived from **k5 polysaccharide** having high anticoagulant and antithrombotic activities and process for their prepn.)

IT **9002-04-4**, Factor IIa **9002-05-5, Factor Xa**
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(inhibition of; **glycosaminoglycans** derived from **k5** **polysaccharide** having high anticoagulant and antithrombotic activities and process for their prepn.)

IT **9000-94-6, Antithrombin III**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(binding to; **glycosaminoglycans** derived from **k5** **polysaccharide** having high anticoagulant and antithrombotic activities and process for their prepn.)
RN 9000-94-6 HCAPLUS
CN Antithrombin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **7782-77-6**, Nitrous acid
RL: RCT (Reactant); RACT (Reactant or reagent)
(degrdn. with; **glycosaminoglycans** derived from **k5** **polysaccharide** having high anticoagulant and antithrombotic activities and process for their prepn.)
RN 7782-77-6 HCAPLUS
CN Nitrous acid (8CI, 9CI) (CA INDEX NAME)

IT **112567-86-9**, Heparin precursor glucuronate 5-**epimerase**
RL: BCP (Biochemical process); CAT (Catalyst use); BIOL (Biological study); PROC (Process); USES (Uses)
(**glycosaminoglycans** derived from **k5** **polysaccharide** having high anticoagulant and antithrombotic activities and process for their prepn.)
RN 112567-86-9 HCAPLUS
CN Epimerase, heparosan N-sulfate D-glucuronosyl 5- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **7773-01-5, Manganese chloride** (**MnCl2**) **7786-30-3, Magnesium chloride** (**MgCl2**), uses **10043-52-4, Calcium chloride** (**CaCl2**), uses **10361-37-2, Barium chloride** (**BaCl2**), uses **14127-61-8, Calcium**(2+), uses **16397-91-4, Manganese**(2+), uses **22537-22-0, Magnesium**(2+), uses **22541-12-4, Barium**(2+), uses
RL: NUU (Other use, unclassified); USES (Uses)
(**glycosaminoglycans** derived from **k5** **polysaccharide** having high anticoagulant and antithrombotic activities and process for their prepn.)
RN 7773-01-5 HCAPLUS
CN Manganese chloride (MnCl2) (8CI, 9CI) (CA INDEX NAME)

RN 7786-30-3 HCAPLUS
CN Magnesium chloride (MgCl2) (9CI) (CA INDEX NAME)

RN 10043-52-4 HCAPLUS
CN Calcium chloride (CaCl2) (9CI) (CA INDEX NAME)

Cl—Ca—Cl

RN 10361-37-2 HCAPLUS
CN Barium chloride (BaCl2) (9CI) (CA INDEX NAME)

Cl—Ba—Cl

RN 14127-61-8 HCAPLUS
CN Calcium, ion (Ca2+) (8CI, 9CI) (CA INDEX NAME)

Ca^{2+}

RN 16397-91-4 HCAPLUS
CN Manganese, ion (Mn2+) (8CI, 9CI) (CA INDEX NAME)

Mn^{2+}

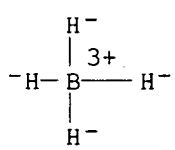
RN 22537-22-0 HCAPLUS
CN Magnesium, ion (Mg2+) (8CI, 9CI) (CA INDEX NAME)

Mg^{2+}

RN 22541-12-4 HCAPLUS
CN Barium, ion (Ba2+) (8CI, 9CI) (CA INDEX NAME)

Ba^{2+}

IT **16940-66-2, Sodium borohydride**
26412-87-3, Pyridine sulfur trioxide **42615-44-1**,
k5 Polysaccharide
RL: RCT (Reactant); RACT (Reactant or reagent)
(**glycosaminoglycans** derived from **k5**
polysaccharide having high anticoagulant and antithrombotic
activities and process for their prepn.)
RN 16940-66-2 HCAPLUS
CN Borate(1-), tetrahydro-, sodium (8CI, 9CI) (CA INDEX NAME)



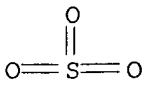
Na^{+}

RN 26412-87-3 HCAPLUS

CN Sulfur trioxide, compd. with pyridine (1:1) (9CI) (CA INDEX NAME)

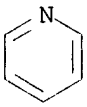
CM 1

CRN 7446-11-9
CMF O3 S



CM 2

CRN 110-86-1
CMF C5 H5 N



RN 42615-44-1 HCAPLUS
CN K 5 (polysaccharide) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **9002-04-4**, Factor IIa **9002-05-5**, **Factor Xa**
RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibition of; **glycosaminoglycans** derived from **k5 polysaccharide** having high anticoagulant and antithrombotic activities and process for their prepn.)
RN 9002-04-4 HCAPLUS
CN Thrombin (8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 9002-05-5 HCAPLUS
CN Blood-coagulation factor Xa (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L102 ANSWER 4 OF 31 HCAPLUS COPYRIGHT 2002 ACS
AN 2002:209601 HCAPLUS
DN 137:29702
TI Identification and molecular cloning of a heparosan synthase from Pasteurella multocida type D
AU DeAngelis, Paul L.; White, Carissa L.
CS Department of Biochemistry and Molecular Biology, Oklahoma Center for Medical Glycobiology, University of Oklahoma Health Sciences Center, Oklahoma City, OK, 73104, USA
SO Journal of Biological Chemistry (2002), 277(9), 7209-7213
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
CC 7-2 (Enzymes)
Section cross-reference(s): 3, 10
AB Pasteurella multocida Type D, a causative agent of atrophic rhinitis in swine and pasteurellosis in other domestic animals, produces an

extracellular **polysaccharide** capsule that is a putative virulence factor. It was reported previously that the capsule was removed by treating microbes with heparin lyase III. We molecularly cloned a 617-residue enzyme, pmHS, which is a heparosan (nonsulfated, **unepimerized** heparin) synthase. Recombinant Escherichia coli-derived pmHS catalyzes the polymn. of the **monosaccharides** from UDP-GlcNAc and UDP-GlcUA. Other structurally related sugar nucleotides did not substitute. Synthase activity was stimulated about 7-25-fold by the addn. of an exogenous polymer acceptor. Mols. composed of .apprx.500-3,000 sugar residues were produced in vitro. The **polysaccharide** was sensitive to the action of heparin lyase III but resistant to hyaluronan lyase. The sequence of the pmHS enzyme is not very similar to the vertebrate heparin/heparan sulfate glycosyltransferases, EXT1 and 2, or to other Pasteurella **glycosaminoglycan** synthases that produce hyaluronan or chondroitin. The pmHS enzyme is the first microbial dual-action glycosyltransferase to be described that forms a **polysaccharide** composed of .beta.4GlcUA-.alpha.4GlcNAc **disaccharide** repeats. In contrast, heparosan biosynthesis in E. coli **K5** requires at least two sep. polypeptides, KfiA and KfiC, to catalyze the same polymn. reaction.

ST heparosan synthase Pasteurella sequence polymn UDPGlcUA UDPGlcNAc

IT DNA sequences
Pasteurella multocida
Protein sequences
(identification and mol. cloning of a heparosan synthase from Pasteurella multocida type D)

IT 423776-68-5 423776-69-6
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(amino acid sequence; identification and mol. cloning of a heparosan synthase from Pasteurella multocida type D)

IT 528-04-1 2616-64-0, UDP-glucuronic acid 152324-79-3, Heparosan
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(identification and mol. cloning of a heparosan synthase from Pasteurella multocida type D)

IT 437767-57-2, Heparosan synthase
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(identification and mol. cloning of a heparosan synthase from Pasteurella multocida type D)

IT 407530-66-9, GenBank AF425591 407531-23-1, GenBank AF439804
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(nucleotide sequence; identification and mol. cloning of a heparosan synthase from Pasteurella multocida type D)

RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD

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L102 ANSWER 5 OF 31 HCAPLUS COPYRIGHT 2002 ACS
AN 2001:878933 HCAPLUS
DN 136:247797
TI Generation of anti-**factor Xa** active, 3-O-sulfated glucosamine-rich sequences by controlled desulfation of oversulfated heparins
AU Naggi, Annamaria; De Cristofano, Barbara; Bisio, Antonella; Torri, Giangiacomo; Casu, Benito
CS G. Ronzoni Institute for Chemical and Biochemical Research, Milan, I-20133, Italy
SO Carbohydrate Research (2001), 336(4), 283-290
CODEN: CRBRAT; ISSN: 0008-6215
PB Elsevier Science Ltd.
DT Journal
LA English
CC 33-8 (Carbohydrates)
Section cross-reference(s): 6
AB In the framework of a project aimed at generating heparin-like sulfation patterns and biol. activities in biotechnol. **glycosaminoglycans**, different approaches have been considered for simulating the .alpha.(1 4)-linked 2-O-sulfated L-**iduronic** acid (IdoA2SO3) N,6-O-sulfated D-glucosamine (GlcNSO36SO3) **disaccharide** sequences prevalent in mammalian heparins. Since the direct approach of sulfating totally O-desulfated heparins, taken as model compds. for C-5-**epimerized** sulfaminoheparosan (N-deacetylated, N-sulfated Escherichia coli **K5 polysaccharide**), preferentially afforded heparins O-sulfated at C-3 instead than at C-2 of the **iduronate** residues, leading to products with low anticoagulant activities, the problem of re-generating a substantial proportion of the original IdoA2SO3 residues was circumvented by performing controlled solvolytic desulfation (with 9:1 vol./vol. **DMSO-MeOH**) of extensively sulfated heparins. The order of desulfation of major residues of heparin GlcN and IdoA and of the minor one D-**glucuronic** acid was: GlcNSO3>GlcN6SO3>IdoA3SO3.simeq.GlcA2SO3.simeq.GlcN3SO3>IdoA2SO3.simeq.GlcA3SO3. Starting from a 'supersulfated' low-mol. wt. heparin, we obtained products with up to 40% of **iduronate** residues O-sulfated exclusively at C-2 and up to 40% of their glucosamine residues O-sulfated at both C-6 and C-3. Upon re-N-sulfation, these products displayed an in vitro antithrombotic activity (expressed as anti-**factor Xa** units) comparable with those of current low-mol. wt. heparins.
ST heparin sulfation desulfation antithrombotic activity
IT **Sulfation**
(prepn. of anti-**factor Xa** active 3-O-sulfated glucosamine rich sequences by controlled desulfation of oversulfated heparins)
IT Polysaccharides, preparation
Uronic acids
RL: PAC (Pharmacological activity); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of anti-**factor Xa** active 3-O-sulfated glucosamine rich sequences by controlled desulfation of oversulfated heparins)
IT Natural products
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP

(Preparation); RACT (Reactant or reagent)
(prepn. of anti-**factor Xa** active 3-O-sulfated glucosamine rich sequences by controlled desulfation of oversulfated heparins)
IT **Sulfation**
(retrosulfation; prepn. of anti-**factor Xa** active 3-O-sulfated glucosamine rich sequences by controlled desulfation of oversulfated heparins)
IT 9005-49-6DP, Heparin, oversulfation and desulfation of
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of anti-**factor Xa** active 3-O-sulfated glucosamine rich sequences by controlled desulfation of oversulfated heparins)
RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
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L102 ANSWER 6 OF 31 HCAPLUS COPYRIGHT 2002 ACS
AN 2001:840398 HCAPLUS
DN 136:167613
TI Toward a biotechnological heparin through combined chemical and enzymatic modification of the Escherichia coli **K5 polysaccharide**
AU Naggi, Annamaria; Torri, Giangiacomo; Casu, Benito; **Oreste, Pasqua**; **Zoppetti, Giorgio**; Li, Jin-Ping; Lindahl, Ulf
CS G. Ronzoni Institute for Chemical and Biochemical Research, Milan, Italy
SO Seminars in Thrombosis and Hemostasis (2001), 27(5), 437-443
CODEN: STHMBV; ISSN: 0094-6176
PB Thieme Medical Publishers, Inc.
DT Journal
LA English
CC 33-8 (**Carbohydrates**)
Section cross-reference(s): 1, 7, 9, 10
AB A process to generate **glycosaminoglycans** with heparin and heparan sulfate-like sequences from the Escherichia coli **K5** capsular **polysaccharide** is described. This polymer has the same structure as N-acetylheparosan, the precursor in heparin/heparan sulfate biosynthesis. The process involves chem. N-deacetylation and N-sulfation, enzymic conversion of up to 60% of the D-**glucuronic** acid to L-**iduronic** acid residues, and chem. O-sulfation. Because direct

sulfation afforded unwanted 3-O-sulfated (instead of 2-O-sulfated) **iduronic** acid residues, a strategy involving graded solvolytic desulfation of chem. over-sulfated C5-**epimerized** sulfaminoheparosans was assessed using persulfated heparin and heparan sulfate as model compds. The O-desulfation process was shown to increase the anti-**factor Xa** activity of over-sulfated heparin.

ST heparan sulfate desulfation antifactor **polysaccharide** prepn enzymic; antithrombin sulfated heparin desulfation antifactor **polysaccharide** prepn enzymic; sulfated heparin desulfation antifactor Xa **polysaccharide K5** Escherichia coli; heparin enzymic modification **polysaccharide** Escherichia coli uronate sulfation desulfation

IT **Polysaccharides**, preparation
RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(capsular; toward a biotechnol. heparin through combined chem. and enzymic modification of the Escherichia coli **K5** **polysaccharide**)

IT **Sulfation**
(retrosulfation; toward a biotechnol. heparin through combined chem. and enzymic modification of the Escherichia coli **K5** **polysaccharide**)

IT Escherichia coli
Sulfation
(toward a biotechnol. heparin through combined chem. and enzymic modification of the Escherichia coli **K5** **polysaccharide**)

IT Uronic acids
RL: BPN (Biosynthetic preparation); NPO (Natural product occurrence); RCT (Reactant); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); RACT (Reactant or reagent)
(toward a biotechnol. heparin through combined chem. and enzymic modification of the Escherichia coli **K5** **polysaccharide**)

IT **42615-44-1P, K5 Polysaccharide**
RL: BPN (Biosynthetic preparation); NPO (Natural product occurrence); RCT (Reactant); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); RACT (Reactant or reagent)
(Escherichia coli; toward a biotechnol. heparin through combined chem. and enzymic modification of the Escherichia coli **K5** **polysaccharide**)

IT 9005-49-6DP, Heparin, desulfated derivs. 9005-49-6P, Heparin, preparation 9050-30-0P, Heparan sulfate
RL: BPN (Biosynthetic preparation); NPO (Natural product occurrence); RCT (Reactant); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); RACT (Reactant or reagent)
(toward a biotechnol. heparin through combined chem. and enzymic modification of the Escherichia coli **K5** **polysaccharide**)

IT **9000-94-6**, Antithrombin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(toward a biotechnol. heparin through combined chem. and enzymic modification of the Escherichia coli **K5** **polysaccharide**)

IT 204784-24-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(toward a biotechnol. heparin through combined chem. and enzymic modification of the Escherichia coli **K5** **polysaccharide**)

RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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IT **42615-44-1P, K5 Polysaccharide**
RL: BPN (Biosynthetic preparation); NPO (Natural product occurrence); RCT (Reactant); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); RACT (Reactant or reagent)
(Escherichia coli; toward a biotechnol. heparin through combined chem. and enzymic modification of the Escherichia coli **K5 polysaccharide**)
RN 42615-44-1 HCAPLUS
CN K 5 (polysaccharide) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT **9000-94-6**, Antithrombin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(toward a biotechnol. heparin through combined chem. and enzymic modification of the Escherichia coli **K5 polysaccharide**)
RN 9000-94-6 HCAPLUS
CN Antithrombin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L102 ANSWER 7 OF 31 HCAPLUS COPYRIGHT 2002 ACS
AN 2001:817859 HCAPLUS
DN 136:128792
TI Fibroblast growth factor-2 antagonist activity and angiostatic capacity of sulfated Escherichia coli **K5 polysaccharide** derivatives
AU Leali, Daria; Belleri, Mirella; Urbinati, Chiara; Coltrini, Daniela; **Oreste, Pasqua; Zoppetti, Giorgio**; Ribatti, Domenico; Rusnati, Marco; Presta, Marco
CS Unit of General Pathology and Immunology, Department of Biomedical Sciences and Biotechnology, School of Medicine, University of Brescia, Brescia, 25123, Italy
SO Journal of Biological Chemistry (2001), 276(41), 37900-37908
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
CC 1-8 (Pharmacology)

AB The angiogenic basic fibroblast growth factor (FGF2) interacts with tyrosine kinase receptors (FGFRs) and heparan sulfate proteoglycans (HSPGs) in endothelial cells. Here, we report the FGF2 antagonist and antiangiogenic activity of novel sulfated derivs. of the Escherichia coli **K5 polysaccharide**. **K5 polysaccharide** was chem. sulfated in N- and/or O-position after N-deacetylation. O-Sulfated and N,O-sulfated **K5** derivs. with a low degree and a high degree of sulfation compete with heparin for binding to 125I-FGF2 with different potency. Accordingly, they abrogate the formation of the HSPG.cntdot.FGF2.cntdot.FGFR ternary complex, as evidenced by their capacity to prevent FGF2-mediated cell-cell attachment of FGFR1-overexpressing HSPG-deficient Chinese hamster ovary (CHO) cells to wild-type CHO cells. They also inhibited 125I-FGF2 binding to FGFR1-overexpressing HSPG-bearing CHO cells and adult bovine aortic endothelial cells. **K5** derivs. also inhibited FGF2-mediated cell proliferation in endothelial GM 7373 cells and in human umbilical vein endothelial (HUVE) cells. In all these assays, the N-sulfated **K5** deriv. and unmodified **K5** were poorly effective. Also, highly O-sulfated and N,O-sulfated **K5** derivs. prevented the sprouting of FGF2-transfected endothelial FGF2-T-MAE cells in fibrin gel and spontaneous angiogenesis in vitro on Matrigel of FGF2-T-MAE and HUVE cells. Finally, the highly N,O-sulfated **K5** deriv. exerted a potent antiangiogenic activity on the chick embryo chorioallantoic membrane. These data demonstrate the possibility of generating FGF2 antagonists endowed with antiangiogenic activity by specific chem. sulfation of bacterial **K5 polysaccharide**. In particular, the highly N,O-sulfated **K5** deriv. may provide the basis for the design of novel angiostatic compds.

ST fibroblast growth factor antagonist angiostatic Escherichia polysaccharide deriv

IT Angiogenesis inhibitors
Cytotoxic agents
Drug design
Escherichia coli
(fibroblast growth factor-2 antagonist activity and angiostatic capacity of sulfated Escherichia coli **K5** **polysaccharide** derivs.)

IT 106096-93-9, Fibroblast growth factor 2
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(fibroblast growth factor-2 antagonist activity and angiostatic capacity of sulfated Escherichia coli **K5** **polysaccharide** derivs.)

IT 78245-16-6D, Repeating unit of 78245-16-6D, Repeating unit of, O-sulfated derivs. **155732-42-6D**, Repeating unit of **155732-42-6D**, Repeating unit of, O-sulfated derivs.
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fibroblast growth factor-2 antagonist activity and angiostatic capacity of sulfated Escherichia coli **K5** **polysaccharide** derivs.)

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IT **155732-42-6D**, Repeating unit of
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fibroblast growth factor-2 antagonist activity and angiostatic capacity of sulfated Escherichia coli **K5** **polysaccharide** derivs.)

RN 155732-42-6 HCAPLUS

CN .alpha.-D-Glucopyranose, 2-deoxy-4-O-.beta.-D-glucopyranuronosyl-2-(sulfoamino)- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L102 ANSWER 8 OF 31 HCAPLUS COPYRIGHT 2002 ACS

AN 2001:730838 HCAPLUS
DN 135:267246
TI **Glycosaminoglycans** derived from the **k5** **polysaccharide** having high anticoagulant and antithrombotic activity and process for their preparation
IN **Zoppetti, Giorgio; Oreste, Pasqua;** Cipolletti, Giovanni
PA Inalco S.p.A., Italy
SO PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C08B037-10
ICS C08B037-00; A61K031-715
CC 1-8 (Pharmacology)
Section cross-reference(s): **33**
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001072848	A1	20011004	WO 2001-EP3461	20010327 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
IT 2000MI0665	A1	20011001	IT 2000-MI665	20000330 <--
PRAI IT 2000-MI665	A	20000330 <--		

AB **Glycosaminoglycans** derived from the **K5** **polysaccharide** having high anticoagulant and antithrombotic activity obtained by a process comprising the prepn. of the **K5** **polysaccharide** from Escherichia coli, N-deacetylation/N-sulfation, C-5 **epimerization**, supersulfation, selective O-desulfation, selective 6-O sulfation and N-sulfation, wherein said **epimerization** is carried out using the glucuronosyl C-5 **epimerase** enzyme in soln. or in immobilized form in presence of specific **divalent cations**.
ST **glycosaminoglycan k5 polysaccharide** deriv anticoagulant antithrombotic
IT Liver
(bovine, glucuronosyl C-5 **epimerase** of; **glycosaminoglycans** derived from **k5** **polysaccharide** having high anticoagulant and antithrombotic activity and prepn. using sol. or immobilized glucuronosyl C-5 **epimerase** and **divalent cations**)
IT **Cations**
(**divalent; glycosaminoglycans** derived from **k5 polysaccharide** having high anticoagulant and antithrombotic activity and prepn. using sol. or immobilized glucuronosyl C-5 **epimerase** and **divalent cations**)
IT Anticoagulants
Deacetylation
Epimerization
Sulfation
(**glycosaminoglycans** derived from **k5** **polysaccharide** having high anticoagulant and antithrombotic activity and prepn. using sol. or immobilized glucuronosyl C-5 **epimerase** and **divalent cations**)
IT **Glycosaminoglycans**, biological studies

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**glycosaminoglycans** derived from **k5** **polysaccharide** having high anticoagulant and antithrombotic activity and prepn. using sol. or immobilized glucuronosyl C-5 **epimerase** and **divalent cations**)

IT Escherichia coli
(**k5 polysaccharides** from; **glycosaminoglycans** derived from **k5** **polysaccharide** having high anticoagulant and antithrombotic activity and prepn. using sol. or immobilized glucuronosyl C-5 **epimerase** and **divalent cations**)

IT Mast cell
(mastocytoma, murine, glucuronosyl C-5 **epimerase** of; **glycosaminoglycans** derived from **k5** **polysaccharide** having high anticoagulant and antithrombotic activity and prepn. using sol. or immobilized glucuronosyl C-5 **epimerase** and **divalent cations**)

IT Immobilization, biochemical
(of glucuronosyl C-5 **epimerase**; **glycosaminoglycans** derived from **k5 polysaccharide** having high anticoagulant and antithrombotic activity and prepn. using sol. or immobilized glucuronosyl C-5 **epimerase** and **divalent cations**)

IT **Sulfation**
(retrosulfation; **glycosaminoglycans** derived from **k5** **polysaccharide** having high anticoagulant and antithrombotic activity and prepn. using sol. or immobilized glucuronosyl C-5 **epimerase** and **divalent cations**)

IT **9000-94-6, antithrombin III**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(binding to; **glycosaminoglycans** derived from **k5** **polysaccharide** having high anticoagulant and antithrombotic activity and prepn. using sol. or immobilized glucuronosyl C-5 **epimerase** and **divalent cations**)

IT **112567-86-9**, Heparin precursor glucuronate 5-**epimerase**
RL: CAT (Catalyst use); USES (Uses)
(**glycosaminoglycans** derived from **k5** **polysaccharide** having high anticoagulant and antithrombotic activity and prepn. using sol. or immobilized glucuronosyl C-5 **epimerase** and **divalent cations**)

IT **7773-01-5, Manganese chloride (MnCl2**) **7786-30-3, Magnesium chloride (MgCl2)**, uses **10043-52-4, Calcium chloride (CaCl2)**, uses **10361-37-2, Barium chloride (BaCl2)**, uses **14127-61-8, Calcium(2+)**, uses **16397-91-4, Manganese(2+)**, uses **22537-22-0, Magnesium(2+)**, uses **22541-12-4, Barium(2+)**, uses
RL: NUU (Other use, unclassified); USES (Uses)
(**glycosaminoglycans** derived from **k5** **polysaccharide** having high anticoagulant and antithrombotic activity and prepn. using sol. or immobilized glucuronosyl C-5 **epimerase** and **divalent cations**)

IT **42615-44-1, k5 polysaccharide**
RL: RCT (Reactant); RACT (Reactant or reagent)
(**glycosaminoglycans** derived from **k5** **polysaccharide** having high anticoagulant and antithrombotic activity and prepn. using sol. or immobilized glucuronosyl C-5 **epimerase** and **divalent cations**)

IT **9002-04-4**, Factor IIa **9002-05-5, Factor**

Xa
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(inhibition of; **glycosaminoglycans** derived from **k5** **polysaccharide** having high anticoagulant and antithrombotic activity and prepn. using sol. or immobilized glucuronosyl C-5 **epimerase** and **divalent cations**)
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
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(3) Inalco Spa; WO 9614425 A 1996 HCAPLUS
(4) Torri Giangiacomo; WO 9842754 A 1998 HCAPLUS
IT **9000-94-6, antithrombin III**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(binding to; **glycosaminoglycans** derived from **k5** **polysaccharide** having high anticoagulant and antithrombotic activity and prepn. using sol. or immobilized glucuronosyl C-5 **epimerase** and **divalent cations**)
RN 9000-94-6 HCAPLUS
CN Antithrombin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **112567-86-9**, Heparin precursor glucuronate 5-**epimerase**
RL: CAT (Catalyst use); USES (Uses)
(**glycosaminoglycans** derived from **k5** **polysaccharide** having high anticoagulant and antithrombotic activity and prepn. using sol. or immobilized glucuronosyl C-5 **epimerase** and **divalent cations**)
RN 112567-86-9 HCAPLUS
CN Epimerase, heparosan N-sulfate D-glucuronosyl 5- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **7773-01-5, Manganese chloride (MnCl2**) **7786-30-3, Magnesium chloride (MgCl2)**, uses **10043-52-4, Calcium chloride (CaCl2)**, uses **10361-37-2, Barium chloride (BaCl2)**, uses **14127-61-8, Calcium**(2+), uses **16397-91-4, Manganese**(2+), uses **22537-22-0, Magnesium**(2+), uses **22541-12-4, Barium**(2+), uses
RL: NUU (Other use, unclassified); USES (Uses)
(**glycosaminoglycans** derived from **k5** **polysaccharide** having high anticoagulant and antithrombotic activity and prepn. using sol. or immobilized glucuronosyl C-5 **epimerase** and **divalent cations**)
RN 7773-01-5 HCAPLUS
CN Manganese chloride (MnCl2) (8CI, 9CI) (CA INDEX NAME)

Cl—Mn—Cl

RN 7786-30-3 HCAPLUS
CN Magnesium chloride (MgCl2) (9CI) (CA INDEX NAME)

Cl—Mg—Cl

RN 10043-52-4 HCAPLUS
CN Calcium chloride (CaCl2) (9CI) (CA INDEX NAME)

Cl—Ca—Cl

RN 10361-37-2 HCAPLUS
CN Barium chloride (BaCl2) (9CI) (CA INDEX NAME)

Cl—Ba—Cl

RN 14127-61-8 HCAPLUS
CN Calcium, ion (Ca2+) (8CI, 9CI) (CA INDEX NAME)

Ca^{2+}

RN 16397-91-4 HCAPLUS
CN Manganese, ion (Mn2+) (8CI, 9CI) (CA INDEX NAME)

Mn^{2+}

RN 22537-22-0 HCAPLUS
CN Magnesium, ion (Mg2+) (8CI, 9CI) (CA INDEX NAME)

Mg^{2+}

RN 22541-12-4 HCAPLUS
CN Barium, ion (Ba2+) (8CI, 9CI) (CA INDEX NAME)

Ba^{2+}

IT **42615-44-1, k5 polysaccharide**
RL: RCT (Reactant); RACT (Reactant or reagent)
(**glycosaminoglycans** derived from **k5** **polysaccharide** having high anticoagulant and antithrombotic activity and prepn. using sol. or immobilized glucuronosyl C-5 **epimerase** and **divalent cations**)
RN 42615-44-1 HCAPLUS
CN K 5 (polysaccharide) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **9002-04-4**, Factor IIa **9002-05-5, Factor Xa**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(inhibition of; **glycosaminoglycans** derived from **k5** **polysaccharide** having high anticoagulant and antithrombotic activity and prepn. using sol. or immobilized glucuronosyl C-5 **epimerase** and **divalent cations**)
RN 9002-04-4 HCAPLUS
CN Thrombin (8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 9002-05-5 HCAPLUS

CN Blood-coagulation factor Xa (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L102 ANSWER 9 OF 31 HCAPLUS COPYRIGHT 2002 ACS
AN **2001:253540** HCAPLUS
DN **135:30616**
TI Substrate Specificity of the Heparan Sulfate Hexuronic Acid 2-O-Sulfotransferase
AU Rong, Jianhui; Habuchi, Hiroko; Kimata, Koji; Lindahl, Ulf; Kusche-Gullberg, Marion
CS Department of Medical Biochemistry and Microbiology, University of Uppsala, Uppsala, Swed.
SO Biochemistry (2001), 40(18), 5548-5555
CODEN: BICHAW; ISSN: 0006-2960
PB American Chemical Society
DT Journal
LA English
CC 7-3 (Enzymes)
AB The interaction of heparan sulfate with different ligand proteins depends on the precise location of O-sulfate groups in the **polysaccharide** chain. We have previously shown that overexpression in human kidney 293 cells of a mouse mastocytoma 2-O-sulfotransferase (2-OST), previously thought to catalyze the transfer of sulfate from 3'-phosphoadenosine 5'-phosphosulfate to C2 of L-iduronyl residues, preferentially increases the level of 2-O-sulfation of D-glucuronyl units [Rong, J., Habuchi, H., Kimata, K., Lindahl, U., and Kusche-Gullberg, M. (2000) Biochem. J. 346, 463-468]. In the study presented here, we further investigated the substrate specificity of the mouse mastocytoma 2-OST. Different **polysaccharide** acceptor substrates were incubated with cell exts. from 2-OST-transfected 293 cells together with the sulfate donor 3'-phosphoadenosine 5'-phospho[35S]sulfate. Incubations with O-desulfated heparin, predominantly composed of [(4).alpha.IdoA(1)-(4).alpha.GlcNSO3(1)-]n, resulted in 2-O-sulfation of iduronic acid. On the other hand, when an N-sulfated capsular **polysaccharide** from Escherichia coli **K5**, with the structure [(4).beta.GlcA(1)-(4).alpha.GlcNSO3(1)-]n was used as an acceptor, sulfate was transferred almost exclusively to C2 of glucuronic acid. Substrates contg. both iduronic and glucuronic acid residues in about equal proportions strongly favored sulfation of iduronic acid. In agreement with these results, the 2-OST was found to have a .apprx.5-fold higher affinity for iduronic acid-contg. substrate **disaccharide** units (Km .apprx. 3.7 .mu.M) than for glucuronic acid-contg. substrate **disaccharide** units (Km .apprx. 19.3 .mu.M).
ST hexuronic acid sulfotransferase specificity iduronic acid substrate
IT **Sulfation**
(biol.; heparan sulfate 2-O-sulfotransferase displays preferential sulfation of iduronic acid over glucuronic acid in polysaccharide substrates)
IT Molecular recognition
(heparan sulfate 2-O-sulfotransferase displays preferential sulfation of iduronic acid over glucuronic acid in polysaccharide substrates)
IT Michaelis constant
(heparan sulfate 2-O-sulfotransferase shows higher affinity for IdoA-contg. disaccharide units than GlcA-contg. disaccharide units)
IT 187414-11-5, Heparan sulfate 2-O-Sulfotransferase
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(heparan sulfate 2-O-sulfotransferase displays preferential sulfation of iduronic acid over glucuronic acid in polysaccharide substrates)
IT 2073-35-0, L-Iduronic acid 6556-12-3, D-Glucuronic acid 9005-49-6, Heparin, biological studies 9050-30-0, Heparan sulfate
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL

(Biological study); PROC (Process)
(heparan sulfate 2-O-sulfotransferase displays preferential sulfation of iduronic acid over glucuronic acid in polysaccharide substrates)

RE.CNT 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD

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L102 ANSWER 10 OF 31 HCAPLUS COPYRIGHT 2002 ACS
AN 2001:31672 HCAPLUS

DN 134:85171
TI Process for the preparation of the **polysaccharides** k4 and **k5** from Escherichia coli
IN Petrucci, Franco; **Zoppetti, Giorgio; Oreste, Pasqua;** Cipolletti, Giovanni
PA Inalco S.p.A., Italy
SO PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C12P019-26
ICS C12N001-20; C08B037-00
CC 16-2 (Fermentation and Bioindustrial Chemistry)
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001002597	A1	20010111	WO 2000-EP6122	20000630
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
IT 99MI1465	A1	20010102	IT 1999-MI1465	19990702
PRAI IT 1999-MI1465	A	19990702		

AB A process is provided for the prepn. of the **polysaccharides** K4 and **K5** by fermn. of Escherichia coli on a medium composed of defatted soya flour, mineral salts and glucose, or of the dialyzed portion of yeast autolyzate, mineral salts and glucose. Following fermn., the **polysaccharides** were purified from fermn. broth by a process which included centrifugation, ultrafiltration, ethanol pptn., diafiltration and ion exchange chromatog. Thus, 820 mg/L of **K5** and 420 mg/L of K4 were obtained from batch fermns. on a defatted soya flour medium.

ST Escherichia fermn polysaccharide prodn purifn
IT Fermentation
(batch; process for the prepn. of the **polysaccharides** k4 and **k5** from Escherichia coli)
IT **Polysaccharides**, preparation
RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)
(capsular, K4 and **K5**; process for the prepn. of the **polysaccharides** k4 and **k5** from Escherichia coli)
IT Ultrafiltration
(cross-flow, tangential flow; process for the prepn. of the **polysaccharides** k4 and **k5** from Escherichia coli)
IT Ultrafiltration
(diafiltration; process for the prepn. of the **polysaccharides** k4 and **k5** from Escherichia coli)
IT Yeast
(ext., dialyzate from; process for the prepn. of the **polysaccharides** k4 and **k5** from Escherichia coli)
IT Soybean (Glycine max)
(flour, defatted; process for the prepn. of the **polysaccharides** k4 and **k5** from Escherichia coli)
IT Centrifugation
Escherichia coli
Ion exchange chromatography
Precipitation (chemical)
(process for the prepn. of the **polysaccharides** k4 and **k5** from Escherichia coli)

IT Flours and Meals
(soybean, defatted; process for the prepn. of the **polysaccharides** k4 and **k5** from Escherichia coli)
IT 9001-92-7, Protease
RL: BPR (Biological process); BSU (Biological study, unclassified); CAT (Catalyst use); BIOL (Biological study); PROC (Process); USES (Uses)
(process for the prepn. of the **polysaccharides** k4 and **k5** from Escherichia coli)
IT 64-17-5, Ethanol, processes 7647-14-5, Sodium chloride, processes
RL: PEP (Physical, engineering or chemical process); PROC (Process)
(process for the prepn. of the **polysaccharides** k4 and **k5** from Escherichia coli)
RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
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L102 ANSWER 11 OF 31 HCAPLUS COPYRIGHT 2002 ACS
AN 2000:664819 HCAPLUS
DN 134:14611
TI Cleavage of the **antithrombin III** binding site in heparin by heparinases and its implication in the generation of low molecular weight heparin
AU Shriver, Zachary; Sundaram, Mallikarjun; Venkataraman, Ganesh; Fareed, Jawed; Linhardt, Robert; Biemann, Klaus; Sasisekharan, Ram
CS Division of Bioengineering and Environmental Health, Massachusetts Institute of Technology, Cambridge, MA, 02139, USA
SO Proceedings of the National Academy of Sciences of the United States of America (2000), 97(19), 10365-10370
CODEN: PNASA6; ISSN: 0027-8424
PB National Academy of Sciences
DT Journal
LA English
CC 7-2 (Enzymes)
Section cross-reference(s): 6, 13
AB Heparin has been used as a clin. anticoagulant for more than 50 yr, making it one of the most effective pharmacol. agents known. Much of heparin's activity can be traced to its ability to bind **antithrombin III** (AT-III). Low mol. wt. heparin (LMWH), derived from heparin by its controlled breakdown, maintains much of the antithrombotic activity of heparin without many of the serious side effects. The clin. significance of LMWH has highlighted the need to understand and develop chem. or enzymic means to generate it. The primary enzymic tools used for the prodn. of LMWH are the heparinases from Flavobacterium heparinum, specifically heparinases I and II. Using pentasaccharide and hexasaccharide model compds., we show that heparinases I and II, but not heparinase III, cleave the AT-III binding site, leaving only a partially intact site. Furthermore, we show herein that glucosamine 3-O sulfation at the reducing end of a glycosidic linkage imparts resistance to heparinase I, II, and III cleavage. Finally, we examine the biol. and pharmacol. consequences of a heparin oligosaccharide that contains only a partial AT-III binding site. We show that such an oligosaccharide lacks some of the functional attributes of heparin- and heparan sulfate-like **glycosaminoglycans** contg. an intact AT-III site.
ST cleavage **antithrombin III** heparin binding site heparinase I II
IT Oligosaccharides, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)

(AT-10 decasaccharide; functional anal. of AT-10 decasaccharide and comparison to **antithrombin III** binding oligosaccharide)

IT **Sulfation**
(biol.; glucosamine 3-O sulfation of heparin at the reducing end of a glycosidic linkage imparts resistance to heparinase I, II, and III cleavage)

IT Bond cleavage
(cleavage of **antithrombin III** binding site in heparin by heparinases and implication in generation of low mol. wt. heparin)

IT Dissociation constant
(for **antithrombin III** complexes with heparin and oligosaccharides)

IT Molecular association
(of heparin and oligosaccharides with **antithrombin III**)

IT 52227-76-6, Heparitinase
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(I, II; heparinases I and II cleave the **antithrombin III** binding site)

IT **9000-94-6, Antithrombin III**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(cleavage of **antithrombin III** binding site in heparin by heparinases and implication in generation of low mol. wt. heparin)

IT 9005-49-6, Heparin, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(cleavage of **antithrombin III** binding site in heparin by heparinases and implication in generation of low mol. wt. heparin)

IT **309965-46-6 309965-48-8 309965-49-9**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(use of model pentasaccharide and hexasaccharide compds. to study heparin cleavage by heparitinases)

RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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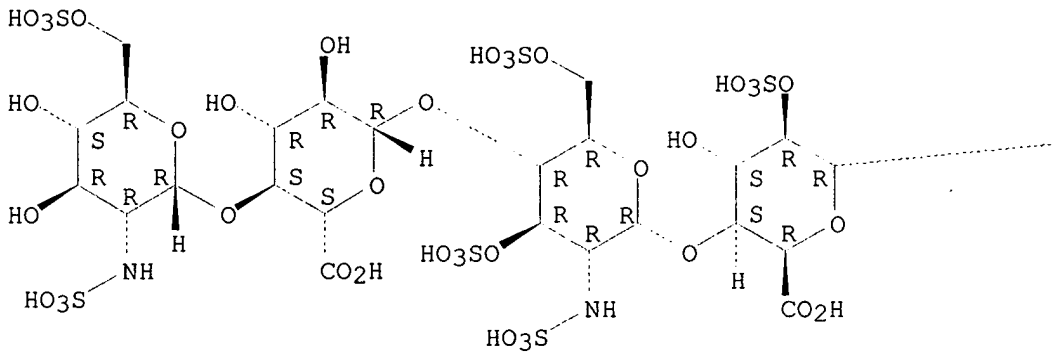
IT **9000-94-6, Antithrombin III**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(cleavage of **antithrombin III** binding site in heparin by heparinases and implication in generation of low mol. wt. heparin)
RN 9000-94-6 HCAPLUS
CN Antithrombin (9CI) (CA INDEX NAME)

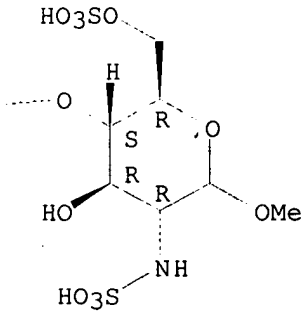
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **309965-46-6 309965-48-8 309965-49-9**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(use of model pentasaccharide and hexasaccharide compds. to study heparin cleavage by heparitinases)
RN 309965-46-6 HCAPLUS
CN D-Glucopyranoside, methyl O-2-deoxy-6-O-sulfo-2-(sulfoamino)-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.4)-O-2-deoxy-3,6-di-O-sulfo-2-(sulfoamino)-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-2-O-sulfo-.alpha.-L-idopyranuronosyl-(1.fwdarw.4)-2-deoxy-2-(sulfoamino)-, 6-(hydrogen sulfate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

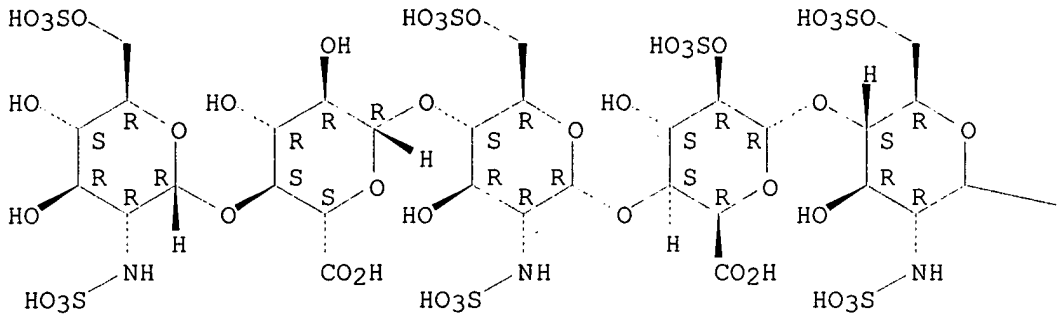


RN 309965-48-8 HCAPLUS
CN D-Glucopyranoside, methyl O-2-deoxy-6-O-sulfo-2-(sulfoamino)-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.4)-O-2-

deoxy-6-O-sulfo-2-(sulfoamino)-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-2-O-sulfo-.alpha.-L-idopyranuronosyl-(1.fwdarw.4)-2-deoxy-2-(sulfoamino)-, 6-(hydrogen sulfate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

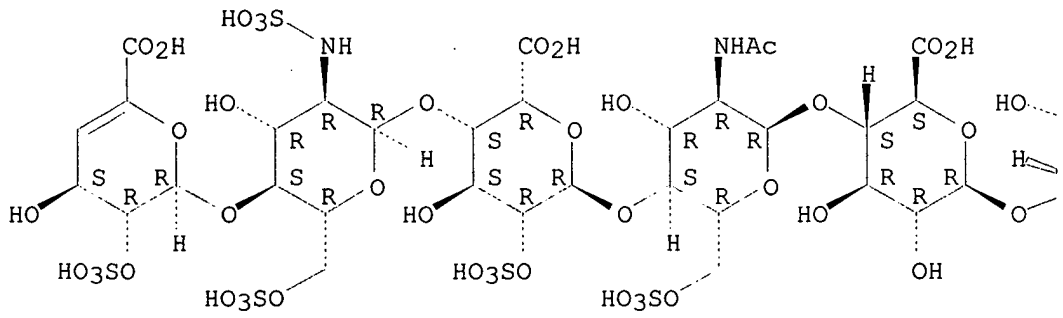
OMe

RN 309965-49-9 HCAPLUS

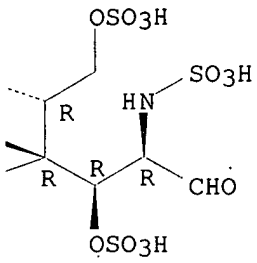
CN D-Glucose, O-4-deoxy-2-O-sulfo-.alpha.-L-threo-hex-4-enopyranuronosyl-(1.fwdarw.4)-O-2-deoxy-6-O-sulfo-2-(sulfoamino)-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-2-O-sulfo-.alpha.-L-idopyranuronosyl-(1.fwdarw.4)-O-2-(acetylamino)-2-deoxy-6-O-sulfo-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.4)-2-deoxy-2-(sulfoamino)-, 3,6-bis(hydrogen sulfate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L102 ANSWER 12 OF 31 HCAPLUS COPYRIGHT 2002 ACS
AN 2000:270488 HCAPLUS
DN 133:27957
TI Biosynthesis of heparin/heparan sulphate: mechanism of **epimerization** of **glucuronyl** C-5
AU Hagner-McWhirter, Asa; Lindahl, Ulf; Li, Jin-Ping
CS Department of Medical Biochemistry and Microbiology, Section for Medical Biochemistry, Biomedical Center, University of Uppsala, Uppsala, SE-751 23, Swed.
SO Biochemical Journal (2000), 347(1), 69-75
CODEN: BIJOAK; ISSN: 0264-6021
PB Portland Press Ltd.
DT Journal
LA English
CC 7-4 (Enzymes)
AB In the biosynthesis of heparin and heparan sulfate, D-**glucuronic** acid residues are converted into L-**iduronic** acid (IdoA) units by C-5 **epimerization**, at the polymer level. The reaction catalyzed by the **epimerase** occurs by reversible abstraction and readdn. of a proton at C-5 of target hexuronic acid residues, through a carbanion intermediate, with or without an inversion of configuration at C-5. Incubation of chem. N-sulfated capsular **polysaccharide** from Escherichia coli **K5** ([4GlcA.beta.1-4GlcNSO3.alpha.1-]n), or of O-desulfated heparin (predominantly [4IdoA.alpha.1-4GlcNSO3.alpha.1-]n) with purified C-5 **epimerase** from bovine liver, resulted in the interconversion of **glucuronic** acid and IdoA residues, which reached equil. (30-40% IdoA/total hexuronic acid) after approx. 1 h of incubation. Similar incubations performed in the presence of 3H2O resulted in progressive labeling at C-5 of the target hexuronic acid units of either substrate **polysaccharide**. Contrary to chem. D-gluco/L-ido equil., established within 1 h of incubation, the accumulation of 3H label continued for at least 6 h. This isotope effect suggests that the second stage of the reaction, i.e. the re-addn. of a proton to the carbanion intermediate, is the rate-limiting step of the overall process. Anal. of the 5-3H-labeled **polysaccharide** products showed that the 3H was approx. equally distributed between **glucuronic** acid and IdoA units, irresp. of incubation time (from 15 min to 72 h) and of the relative proportions of the two epimers in the substrate. This finding points to a catalytic mechanism in which the abstraction and re-addn. of C-5 protons are effected by two polyprotic bases, presumably lysine residues. Previous expts. relating to the biosynthesis of dermatan sulfate were similarly interpreted in terms of a two-base **epimerization** mechanism but differed from the present findings by implicating one monoprotic and one polyprotic base function.
ST heparin heparan sulfate formation **glucuronyl** C5 **epimerization** mechanism
IT **Epimerization**

(biosynthesis of heparin/heparan sulfate: mechanism of **epimerization** of **glucuronyl** C-5)

IT **37342-00-0, Epimerase**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(C-5; biosynthesis of heparin/heparan sulfate: mechanism of **epimerization** of **glucuronyl** C-5)

IT 2073-35-0, L-**Iduronic** acid 6556-12-3, D-**Glucuronic** acid
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(biosynthesis of heparin/heparan sulfate: mechanism of **epimerization** of **glucuronyl** C-5)

IT 9005-49-6, Heparin, biological studies 9050-30-0, Heparan sulfate
RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(biosynthesis of heparin/heparan sulfate: mechanism of **epimerization** of **glucuronyl** C-5)

RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD

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IT **37342-00-0, Epimerase**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(C-5; biosynthesis of heparin/heparan sulfate: mechanism of

epimerization of **glucuronyl** C-5)
RN 37342-00-0 HCAPLUS
CN Epimerase (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L102 ANSWER 13 OF 31 HCAPLUS COPYRIGHT 2002 ACS
AN 2000:108077 HCAPLUS
DN 132:262013
TI Biosynthesis of heparin/heparan sulfate: kinetic studies of the glucuronyl C5-**epimerase** with N-sulfated derivatives of the Escherichia coli **K5** capsular **polysaccharide** as substrates
AU Hagner-McWhirter, Asa; Hannesson, Helgi H.; Campbell, Patrick; Westley, John; Roden, Lennart; Lindahl, Ulf; Li, Jin-Ping
CS Department of Medical Biochemistry and Microbiology, The Biomedical Center, Uppsala University, Uppsala, S-751 23, Swed.
SO Glycobiology (2000), 10(2), 159-171
CODEN: GLYCE3; ISSN: 0959-6658
PB Oxford University Press
DT Journal
LA English
CC 7-3 (Enzymes)
Section cross-reference(s): 6
AB The D-glucuronyl C5-**epimerase** involved in the biosynthesis of heparin and heparan sulfate was investigated with focus on its substrate specificity, its kinetic properties, and a comparison of **epimerase** prepns. from the Furth mastocytoma and bovine liver, which synthesize heparin and heparan sulfate, resp. New substrates for the **epimerase** were prepd. from the capsular **polysaccharide** of Escherichia coli **K5**, which had been labeled at C5 of its D-glucuronic and N-acetyl-D-glucosamine moieties by growing the bacteria in the presence of D-[5-3H]glucose. Following complete or partial (.apprx.50%) N-deacetylation of the **polysaccharide** by hydrazinolysis, the free amino groups were sulfated by treatment with trimethylamine.cntdot.SO3 complex, which yielded products that were recognized as substrates by the **epimerase** and released tritium from C5 of the D-glucuronyl residues upon incubation with the enzyme. Comparison of the kinetic properties of the two substrates showed that the fully N-sulfated deriv. was the best substrate in terms of its Km value, which was significantly lower than that of its partially N-acetylated counterpart. The Vmax values for the E.coli **polysaccharide** derivs. were essentially the same but were both lower than that of the O-desulfated [3H]heparin used in our previous studies. Surprisingly, the apparent Km values for all three substrates increased with increasing enzyme concn. The reason for this phenomenon is not entirely clear at present. Partially purified C5-**epimerase** prepns. from the Furth mastocytoma and bovine liver, resp., behaved similarly in terms of their reactivity towards the various substrates, but the variation in apparent Km values with enzyme concn. precluded a detailed comparison of their kinetic properties.
ST glucuronyl C5 **epimerase** heparin heparan sulfate capsular polysaccharides
IT Enzyme kinetics
Michaelis constant
(kinetic studies of the glucuronyl C5-**epimerase** with N-sulfated derivs. of the Escherichia coli **K5** capsular **polysaccharides**)
IT **Polysaccharides**, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(sulfated, **K5**; participation of glucuronyl C5 **epimerase** in biosynthesis of heparin/heparan sulfate)
IT **112567-86-9**, Heparan precursor glucuronate 5-**epimerase**

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(kinetic studies of the glucuronyl C5-**epimerase** with N-sulfated derivs. of the Escherichia coli **K5** capsular **polysaccharides**)

IT 9005-49-6D, Heparin, O-desulfated, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(kinetic studies of the glucuronyl C5-**epimerase** with N-sulfated derivs. of the Escherichia coli **K5** capsular **polysaccharides**)

IT 9050-30-0, Heparan sulfate
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(participation of glucuronyl C5 **epimerase** in biosynthesis of heparin/heparan sulfate)

RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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IT **112567-86-9**, Heparan precursor glucuronate 5-**epimerase**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(kinetic studies of the glucuronyl C5-**epimerase** with N-sulfated derivs. of the Escherichia coli **K5** capsular **polysaccharides**)

RN 112567-86-9 HCAPLUS
CN Epimerase, heparosan N-sulfate D-glucuronosyl 5- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L102 ANSWER 14 OF 31 HCAPLUS COPYRIGHT 2002 ACS
AN 1998:550445 HCAPLUS
DN 129:177144
TI O-Sulfated bacterial polysaccharides
IN **Zoppetti, Giorgio; Oreste, Pasqua;** Cipolletti, Giovanni
PA Inalco S.p.A., Italy
SO PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C08B037-00
ICS A61K031-725; A61K007-48
CC 44-5 (Industrial **Carbohydrates**)
Section cross-reference(s): **33**, 62, 63
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9834958	A1	19980813	WO 1998-EP598	19980204
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9863943	A1	19980826	AU 1998-63943	19980204
	AU 723168	B2	20000817		
	EP 958307	A1	19991124	EP 1998-909387	19980204
	EP 958307	B1	20020102		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2001510502	T2	20010731	JP 1998-533750	19980204
	AT 211488	E	20020115	AT 1998-909387	19980204
	ES 2169503	T3	20020701	ES 1998-909387	19980204
	US 6288044	B1	20010911	US 1999-355211	19990723
PRAI	IT 1997-MI252	A	19970207		
	WO 1998-EP598	W	19980204		

AB A process is disclosed for the prepn. of O-sulfated K4, **K5** and K40 **polysaccharides** useful for the treatment of tumoral, HIV-1 and coagulation pathologies and in cosmetic prepns., wherein the K4, **K5** or K40 **polysaccharide** in the form of sodium salt is suspended in an aprotic solvent and directly submitted to the reaction of O-sulfation with a pyridine-sulfur trioxide or trimethylamine-sulfur trioxide adduct or with chlorosulfonic acid.
ST sulfation bacterial polysaccharide; sulfate ester polysaccharide cosmetic prepn; HIV treatment bacterial polysaccharide sulfate; tumor treatment bacterial polysaccharide sulfate; coagulation pathol bacterial polysaccharide sulfate; glucuronoglucosamine bacterial polysaccharide sulfate
IT Hair preparations
(growth stimulants; manuf. of sulfated bacterial polysaccharides)
IT Anti-AIDS agents
Antitumor agents
Coagulation
Cosmetics
Sulfation

(manuf. of sulfated bacterial polysaccharides)
IT Polysaccharides, preparation
RL: BUU (Biological use, unclassified); IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(manuf. of sulfated bacterial polysaccharides)
IT **17736-86-6**, Sulfur trioxide, compd. with trimethylamine
28322-92-1, Sulfur trioxide, compd. with pyridine
RL: RCT (Reactant); RACT (Reactant or reagent)
(manuf. of sulfated bacterial polysaccharides)
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Akzo N V; EP 0333243 A 1989 HCAPLUS
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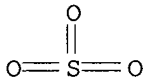
IT **17736-86-6**, Sulfur trioxide, compd. with trimethylamine
28322-92-1, Sulfur trioxide, compd. with pyridine
RL: RCT (Reactant); RACT (Reactant or reagent)
(manuf. of sulfated bacterial polysaccharides)
RN 17736-86-6 HCAPLUS
CN Methanamine, N,N-dimethyl-, compd. with sulfur trioxide (9CI) (CA INDEX NAME)

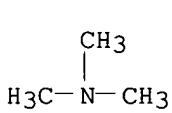
CM 1

CRN 7446-11-9
CMF O3 S



CM 2

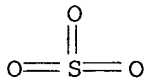
CRN 75-50-3
CMF C3 H9 N



RN 28322-92-1 HCAPLUS
CN Sulfur trioxide, compd. with pyridine (8CI, 9CI) (CA INDEX NAME)

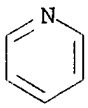
CM 1

CRN 7446-11-9
CMF O3 S



CM 2

CRN 110-86-1
CMF C5 H5 N



L102 ANSWER 15 OF 31 HCAPLUS COPYRIGHT 2002 ACS
AN 1998:515824 HCAPLUS
DN 129:185989
TI Substrate specificity of heparanases from human hepatoma and platelets
AU Pikas, Dagmar Sandback; Li, Jin-Ping; Vlodavsky, Israel; Lindahl, Ulf
CS Department of Medical Biochemistry and Microbiology, Uppsala University, Uppsala, S-751 23, Swed.
SO Journal of Biological Chemistry (1998), 273(30), 18770-18777
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
CC 7-3 (Enzymes)
Section cross-reference(s): 14
AB Heparan sulfate proteoglycans, attached to cell surfaces or in the extracellular matrix, interact with a multitude of proteins via their heparan sulfate side chains. Degrdn. of these chains by limited (endoglycosidic) heparanase cleavage is believed to affect a variety of biol. processes. Although the occurrence of heparanase activity in mammalian tissues has been recognized for many years, the mol. characteristics and substrate recognition properties of the enzyme(s) have remained elusive. In the present study, the substrate specificity and cleavage site of heparanase from human hepatoma and platelets were investigated. Both enzyme prepns. were found to cleave the single .beta.-D-glucuronidic linkage of a heparin **octasaccharide**. A capsular **polysaccharide** from Escherichia coli **K5**, with the same (-GlcUA.beta.1,4-GlcNAc.alpha.1,4-)n structure as the unmodified backbone of heparan sulfate, resisted heparanase degrdn. in its native state as well as after chem. N-deacetylation/N-sulfation or partial enzymic C-5 **epimerization** of .beta.-D-GlcUA to .alpha.-L-IdceA. By contrast, a chem. O-sulfated (but still N-acetylated) **K5** deriv. was susceptible to heparanase cleavage. O-Sulfate groups, but not N-sulfate or IdceA residues, thus are essential for substrate recognition by the heparanase(s). In particular, selective O-desulfation of the heparin **octasaccharide** implicated a 2-O-sulfate group on a hexuronic acid residue located two **monosaccharide** units from the cleavage site, toward the reducing end.
ST heparanase substrate specificity hepatoma platelet human
IT Structure-activity relationship
(enzyme substrate; substrate specificity of heparanases from human hepatoma and platelets)
IT Liver, neoplasm
(hepatoma; substrate specificity of heparanases from human hepatoma and platelets)
IT Platelet (blood)
(substrate specificity of heparanases from human hepatoma and platelets)
IT Functional groups
(sulfate; substrate specificity of heparanases from human hepatoma and platelets)
IT 89800-66-8, Heparanase

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(substrate specificity of heparanases from human hepatoma and platelets)

IT 6556-12-3, D-Glucuronic acid 9005-49-6, Heparin, biological studies 9050-30-0, Heparan sulfate
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(substrate specificity of heparanases from human hepatoma and platelets)

RE.CNT 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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L102 ANSWER 16 OF 31 HCAPLUS COPYRIGHT 2002 ACS
AN **1998:169459** HCAPLUS
DN **128:239470**
TI Semi-synthetic sulphaminoheparosansulfates having high antimetastatic activity and reduced hemorrhagic risk
IN Naggi, Annamaria; Torri, Giangiacomo
PA Istituto Scientifico Di Chimica E Biochimica "G. Ronzoni", Italy; Naggi, Annamaria; Torri, Giangiacomo
SO PCT Int. Appl., 13 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-725
CC 1-6 (Pharmacology)
Section cross-reference(s): 33
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9809636	A1	19980312	WO 1997-EP4682	19970828
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9744561	A1	19980326	AU 1997-44561	19970828
	AU 715868	B2	20000210		
	EP 956027	A1	19991117	EP 1997-942887	19970828
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, FI				
	JP 2000517328	T2	20001226	JP 1998-512201	19970828
	RU 2176915	C2	20011220	RU 1999-106795	19970828
	US 6329351	B1	20011211	US 1999-254128	19991220
PRAI	IT 1996-MI1840	A	19960906		
	WO 1997-EP4682	W	19970828		

AB Sulphaminoheparosansulfates are disclosed which have high antimetastatic activity and low anticoagulant activity. The sulphaminoheparosansulfates are obtainable from the Escherichia coli **K5** **polysaccharide** by deacetylation and subsequent sulfation with sulfuric anhydride/trimethylamine adduct, carried out at 0 .degree.C, for times ranging from 0.25 to 2 h, using a reactant/**polysaccharide** ratio (SO3 equivalents/available OH groups equiv.) of 5.
ST sulphaminoheparosansulfate prepn metastasis inhibitor
IT **Polysaccharides**, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(E. coli **K5**; semi-synthetic sulphaminoheparosansulfates with high antimetastatic activity and low anticoagulant activity)
IT Antitumor agents
(metastasis; semi-synthetic sulphaminoheparosansulfates with high antimetastatic activity and low anticoagulant activity)
IT Blood coagulation
Deacetylation
Escherichia coli
Sulfation
(semi-synthetic sulphaminoheparosansulfates with high antimetastatic activity and low anticoagulant activity)
IT 204784-24-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(semi-synthetic sulphaminoheparosansulfates with high antimetastatic activity and low anticoagulant activity)

L102 ANSWER 17 OF 31 HCAPLUS COPYRIGHT 2002 ACS
AN 1998:74274 HCAPLUS
DN 128:240970
TI A major common trisulfated hexasaccharide core sequence, hexuronic acid(2-sulfate)-glucosamine(N-sulfate)-**iduronic** acid-N-acetylglucosamine-**glucuronic** acid-glucosamine(N-sulfate), isolated from the low sulfated irregular region of porcine intestinal heparin
AU Yamada, Shuhei; Yamane, Yukari; Tsuda, Hiromi; Yoshida, Keiichi; Sugahara, Kazuyuki
CS Department of Biochemistry, Kobe Pharmaceutical University, Kobe, 658, Japan
SO Journal of Biological Chemistry (1998), 273(4), 1863-1871
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
CC 6-4 (General Biochemistry)
AB The major structure of the low sulfated irregular region of porcine intestinal heparin was investigated by characterizing the hexasaccharide fraction prepd. by extensive digestion of the highly sulfated region with Flavobacterium heparinase and subsequent size fractionation by gel chromatog. Structures of a tetrasaccharide, a pentasaccharide, and eight hexasaccharide components in this fraction, which accounted for approx. 19% (wt./wt.) of the starting heparin representing the major oligosaccharide fraction derived from the irregular region, were detd. by chem. and enzymic analyses as well as 1H NMR spectroscopy. Five compds. including one penta- and four hexasaccharides had hitherto unreported structures. The structure of the pentasaccharide with a **glucuronic** acid at the reducing terminus was assumed to be derived from the reducing terminus of a heparin **glycosaminoglycan** chain and may represent the reducing terminus exposed by a tissue endo-.beta.-**glucuronidase** involved in the intracellular post-synthetic fragmentation of macromol. heparin. Eight out of the 10 isolated oligosaccharides shared the trisaccharide sequence, -4IdceA.alpha.1-4Glc-NAc.alpha.1-4GlcA.beta.1-, and its reverse sequence, -4GlcA.beta.1-4GlcNAc.alpha.1-4IdceA.alpha.1-, was not found. The latter has not been reported to date for heparin/heparan sulfate, indicating the substrate specificity of the D-**glucuronyl** C-5 **epimerase**. Furthermore, seven hexasaccharides shared the common trisulfated hexasaccharide core sequence .DELTA.HexA(2-sulfate).alpha.1-4GlcN(N-sulfate).alpha.1-4IdceA.alpha.1-4Gl-cNAc.alpha.1-4GlcA.beta.1-4GlcN(N-sulfate) which contained the above trisaccharide sequence (.DELTA.HexA, IdceA, GlcN, and GlcA represent 4-deoxy-.alpha.-L-threo-hex-4-enepyranosyluronic acid, L-**iduronic** acid, D-glucosamine, and D-**glucuronic** acid, resp.) and addnl. sulfate groups. The specificity of the heparinase used for prepn. of the oligosaccharides indicates the occurrence of the common pentasulfated octasaccharide core sequence, -4GcN(N-sulfate).alpha.1-4HexA(2-sulfate)1-4 GlcN(N-sulfate).alpha.1-4IdceA.alpha.1-4GlcNAc.alpha.1-4GlcA.beta.1-4 GlcN(N-sulfate).alpha.1-4HexA(2-sulfate)1-, where the central hexasaccharide is flanked by GlcN(N-sulfate) and HexA(2-sulfate) on the nonreducing and reducing sides, resp. The revealed common sequence consisted a low sulfated trisaccharide representing the irregular region sandwiched by highly sulfated regions and should reflect the control mechanism of heparin biosynthesis.
ST pig intestinal heparin hexasaccharide core structure
IT Swine
(hexasaccharide core sequence hexuronic acid(2-sulfate)-glucosamine(N-sulfate)-**iduronic** acid-N-acetylglucosamine-**glucuronic**

acid-glucosamine(N-sulfate) from low sulfated irregular region of porcine intestinal heparin)

IT **117305-24-5 139953-16-5** 163231-06-9
177326-74-8 177326-75-9 205049-87-2
205049-88-3 205049-89-4 **205049-90-7**
205049-91-8 205049-92-9
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)
(hexasaccharide core sequence hexuronic acid(2-sulfate)-glucosamine(N-sulfate)-**iduronic** acid-N-acetylglucosamine-**glucuronic** acid-glucosamine(N-sulfate) from low sulfated irregular region of porcine intestinal heparin)

IT 9005-49-6, Heparin, biological studies
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(hexasaccharide core sequence hexuronic acid(2-sulfate)-glucosamine(N-sulfate)-**iduronic** acid-N-acetylglucosamine-**glucuronic** acid-glucosamine(N-sulfate) from low sulfated irregular region of porcine intestinal heparin)

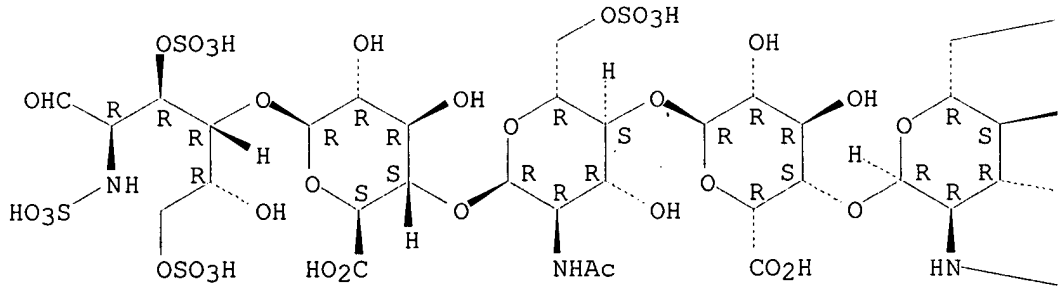
IT **117305-24-5 139953-16-5 177326-74-8**
177326-75-9 205049-87-2 205049-88-3
205049-90-7 205049-91-8 205049-92-9
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)
(hexasaccharide core sequence hexuronic acid(2-sulfate)-glucosamine(N-sulfate)-**iduronic** acid-N-acetylglucosamine-**glucuronic** acid-glucosamine(N-sulfate) from low sulfated irregular region of porcine intestinal heparin)

RN 117305-24-5 HCAPLUS

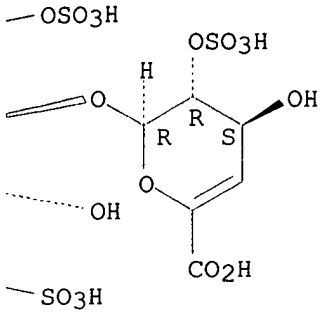
CN D-Glucose, O-4-deoxy-2-O-sulfo-.alpha.-L-threo-hex-4-enopyranuronosyl-(1.fwdarw.4)-O-2-deoxy-6-O-sulfo-2-(sulfoamino)-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-.alpha.-L-idopyranuronosyl-(1.fwdarw.4)-O-2-(acetylamino)-2-deoxy-6-O-sulfo-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.4)-2-deoxy-2-(sulfoamino)-, 3,6-bis(hydrogen sulfate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



RN 139953-16-5 HCAPLUS
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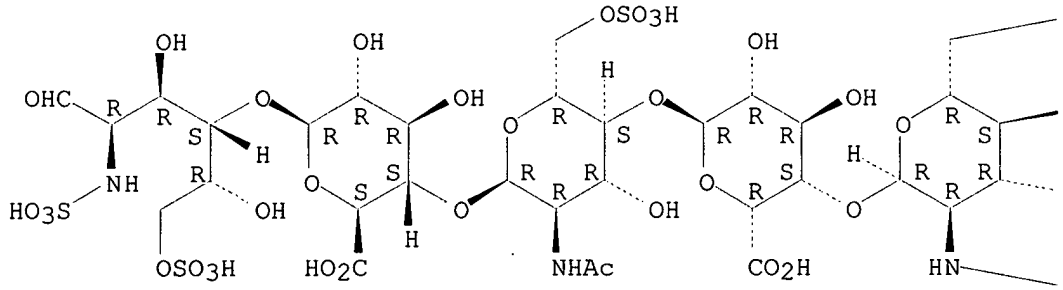
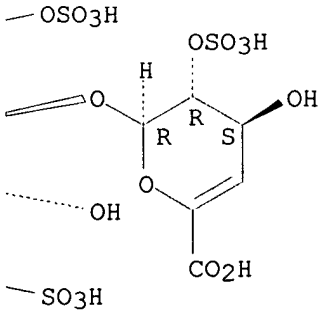
Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



RN 177326-74-8 HCAPLUS
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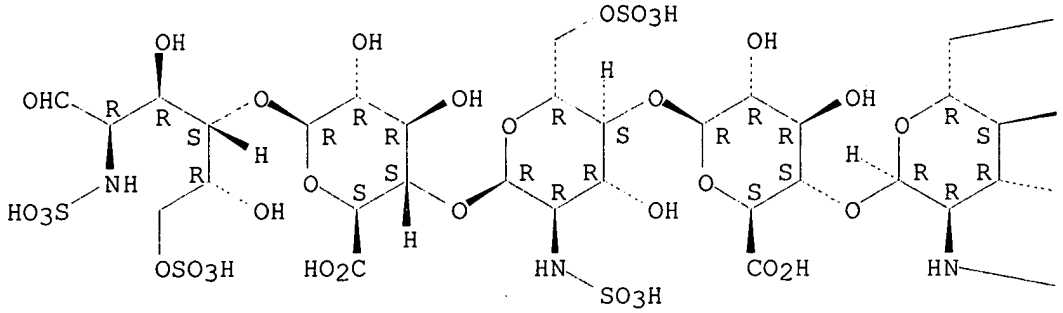
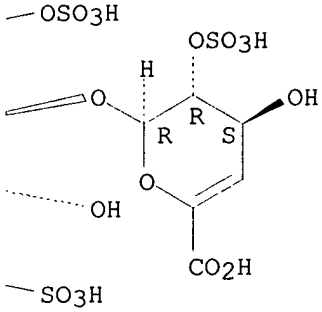
Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



RN 177326-75-9 HCAPLUS
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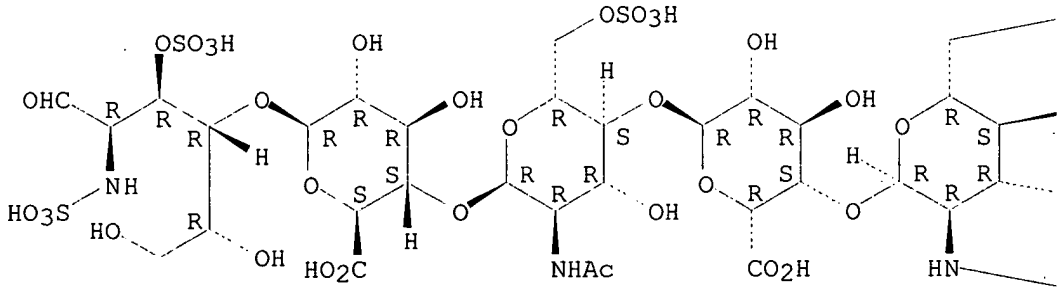
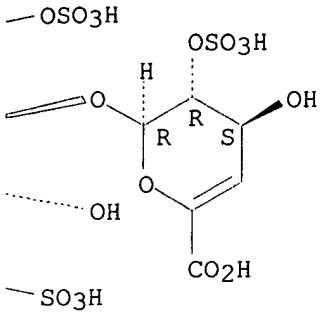
Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



RN 205049-87-2 HCAPLUS
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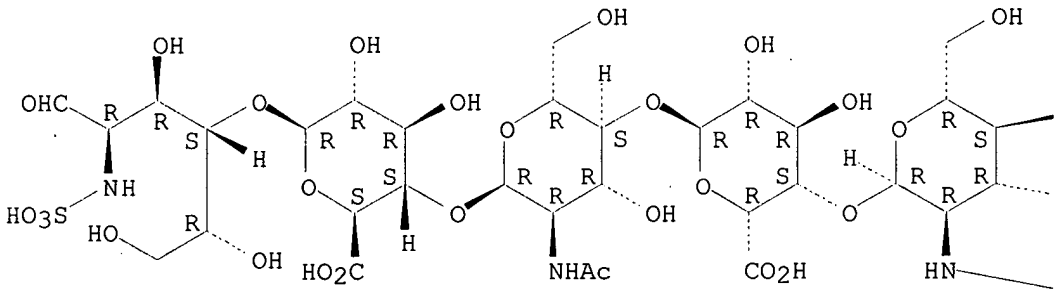
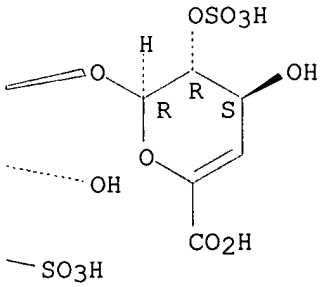
Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



RN 205049-88-3 HCAPLUS
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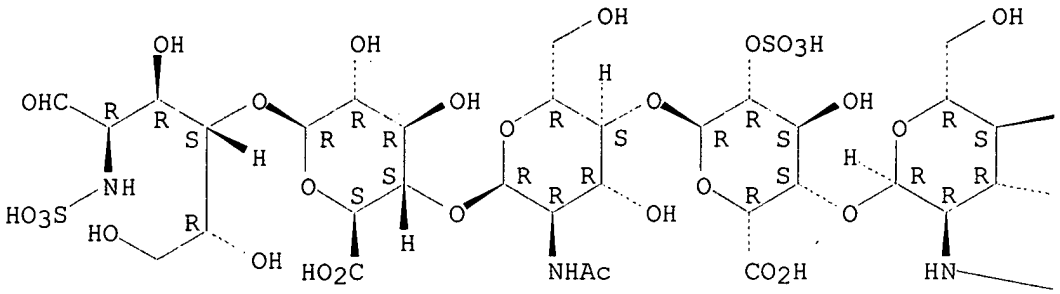
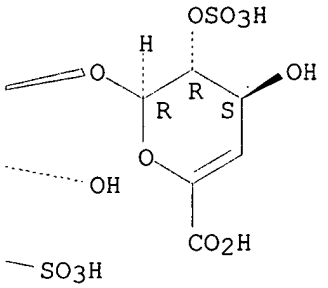
Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



RN 205049-90-7 HCAPLUS
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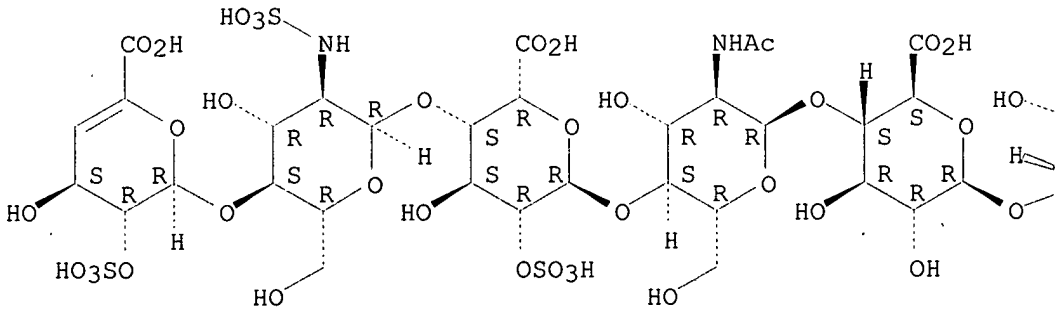
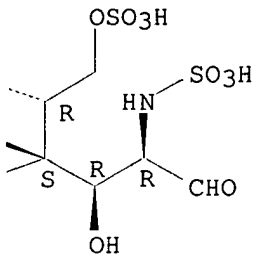
Absolute stereochemistry.

PAGE 1-A



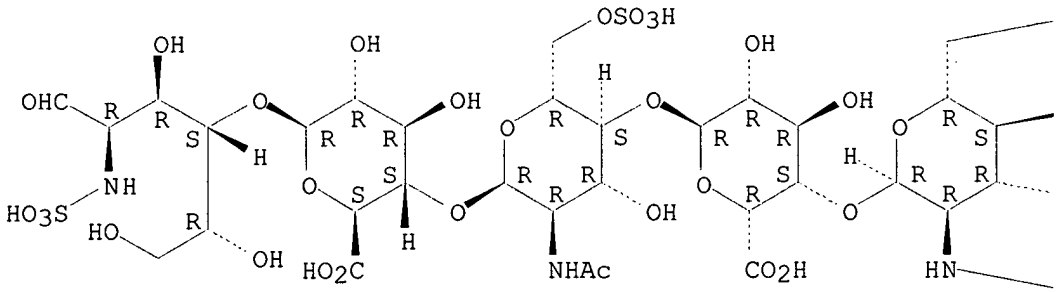
PAGE 1-B



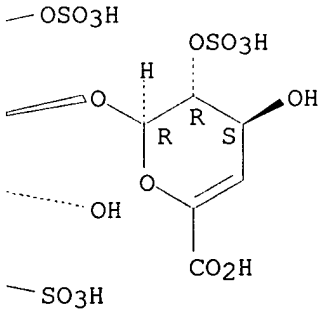
RN 205049-91-8 HCAPLUS
CN D-Glucose, O-4-deoxy-2-O-sulfo-.alpha.-L-threo-hex-4-enopyranuronosyl-(1.fwdarw.4)-O-2-deoxy-6-O-sulfo-2-(sulfoamino)-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-.alpha.-L-idopyranuronosyl-(1.fwdarw.4)-O-2-(acetylamino)-2-deoxy-6-O-sulfo-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.4)-2-deoxy-2-(sulfoamino)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



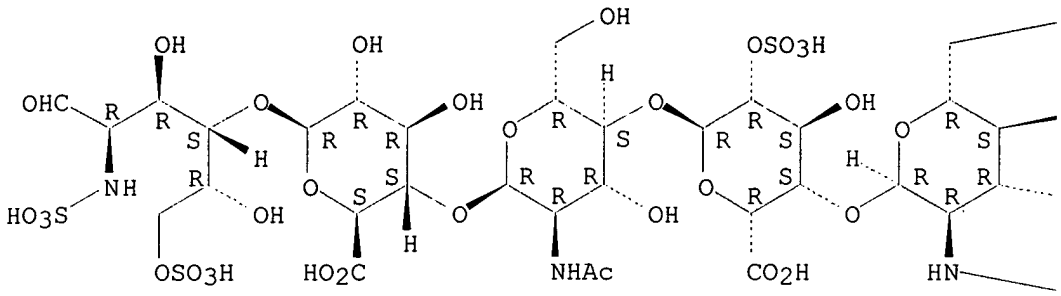
PAGE 1-B



RN 205049-92-9 HCAPLUS
CN D-Glucose, O-4-deoxy-2-O-sulfo-.alpha.-L-threo-hex-4-enopyranuronosyl-(1.fwdarw.4)-O-2-deoxy-6-O-sulfo-2-(sulfoamino)-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-6-O-sulfo-.alpha.-L-idopyranuronosyl-(1.fwdarw.4)-O-2-(acetylamino)-2-deoxy-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.4)-2-deoxy-2-(sulfoamino)-, 6-(hydrogen sulfate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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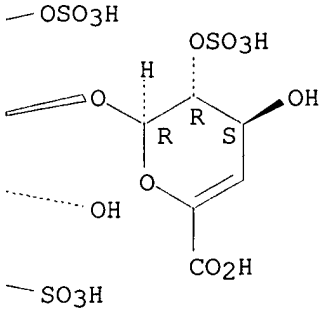
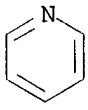


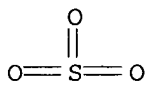
L102 ANSWER 18 OF 31 HCAPLUS COPYRIGHT 2002 ACS
AN 1997:757036 HCAPLUS
DN 128:39636
TI Derivatives of **K5 polysaccharide** having high anticoagulant activity
IN **Zoppetti, Giorgio; Oreste, Pasqua;** Cipolletti, Giovanni
PA Inalco S.P.A., Italy; Zoppetti, Giorgio; Oreste, Pasqua; Cipolletti, Giovanni
SO PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C08B037-00
ICS A61K031-715
CC 63-8 (Pharmaceuticals)
Section cross-reference(s): 1
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9743317	A1	19971120	WO 1997-EP2379	19970509
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9730265	A1	19971205	AU 1997-30265	19970509
EP 897393	A1	19990224	EP 1997-924941	19970509

EP 897393 B1 20011205
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, FI
AT 210154 E 20011215 AT 1997-924941 19970509
ES 2167748 T3 20020516 ES 1997-924941 19970509
US 6162797 A 20001219 US 1998-180406 19981106
PRAI IT 1996-MI956 A 19960510
WO 1997-EP2379 W 19970509
AB Derivs. of the **K5 polysaccharide** having high anticoagulant activity obtained by a process comprising the N-deacetylation of the **K5 polysaccharide** followed by N-sulfation, **epimerization**, O-sulfation and N-resulfation.
ST **polysaccharide K5** anticoagulant
IT **Polysaccharides**, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**K5**; derivs. of **K5 polysaccharide** having high anticoagulant activity)
IT Anticoagulants
Deacetylation
Epimerization
Sulfation
(derivs. of **K5 polysaccharide** having high anticoagulant activity)
IT 68-12-2, Dmf, processes
RL: PEP (Physical, engineering or chemical process); PROC (Process)
(derivs. of **K5 polysaccharide** having high anticoagulant activity)
IT 75-50-3, Trimethylamine, reactions 102-82-9, Tributylamine **110-86-1**, Pyridine, reactions 121-44-8, Triethylamine, reactions **7446-11-9**, Sulfur trioxide, reactions
RL: PEP (Physical, engineering or chemical process); RCT (Reactant); PROC (Process); RACT (Reactant or reagent)
(derivs. of **K5 polysaccharide** having high anticoagulant activity)
IT **110-86-1**, Pyridine, reactions **7446-11-9**, Sulfur trioxide, reactions
RL: PEP (Physical, engineering or chemical process); RCT (Reactant); PROC (Process); RACT (Reactant or reagent)
(derivs. of **K5 polysaccharide** having high anticoagulant activity)
RN 110-86-1 HCAPLUS
CN Pyridine (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



RN 7446-11-9 HCAPLUS
CN Sulfur trioxide (8CI, 9CI) (CA INDEX NAME)



L102 ANSWER 19 OF 31 HCAPLUS COPYRIGHT 2002 ACS
AN 1997:302576 HCAPLUS

DN 127:2882
TI Interaction of HIV-1 Tat protein with heparin. Role of the backbone structure, sulfation, and size
AU Rusnati, Marco; Coltrini, Daniela; **Oreste, Pasqua; Zoppetti, Giorgio;** Albini, Adriana; Noonan, Douglas; Di Fagagna, Fabrizio D'adda; Giacca, Mauro; Presta, Marco
CS Department of Biomedical Sciences and Biotechnology, School of Medicine, Chair of General Pathology and Immunology, University of Brescia, Brescia, 25123, Italy
SO Journal of Biological Chemistry (1997), 272(17), 11313-11320
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
CC 10-2 (Microbial, Algal, and Fungal Biochemistry)
AB Human immunodeficiency virus type 1 (HIV-1) Tat protein is released from infected cells. Extracellular Tat enters the cell where it stimulates the transcriptional activity of HIV-long terminal repeat (LTR) and of endogenous genes. Heparin has been shown previously to modulate the angiogenic activity of extracellular Tat. Heparin binds specifically to recombinant HIV-1 Tat produced as glutathione S-transferase (GST) fusion protein and immobilized on glutathione-agarose beads. Heparin and heparan sulfate (HS), but not dermatan sulfate, chondroitin sulfates A and C, hyaluronic acid, and **K5 polysaccharide**, competed with 3H-labeled heparin for binding to immobilized GST-Tat and inhibited HIV-LTR transactivation induced by extracellular GST-Tat. Selective 2-O-, 6-O-, total-O-desulfation, or N-desulfation/N-acetylation dramatically reduced the capacity of heparin to bind GST-Tat. Totally-O-desulfated and 2-O-desulfated heparins also showed a reduced capacity to inhibit the trans-activating activity of GST-Tat. Very low mol. wt. heparins showed a significant decrease in their capacity to bind GST-Tat and to inhibit its LTR trans-activating activity when compared with conventional 13.6-kDa heparin. However, when 3.0-kDa heparin was affinity chromatographed on immobilized GST-Tat to isolate binding and non-binding subfractions, the Tat-bound fraction was .gtoreq.1,000 times more potent than the unbound fraction in inhibiting the trans-activating activity of GST-Tat. The results demonstrate that Tat interacts in a size-dependent manner with heparin/HS and that high affinity Tat-heparin interaction requires at least some 2-O-, 6-O-, and N-positions to be sulfated. The Tat binding activity of the **glycosaminoglycans** tested correlates with their capacity to affect the trans-activating activity of extracellular Tat, indicating the possibility to design specific heparin/HS-like structures with Tat-antagonist activity.
ST HIV 1 Tat protein heparin sulfation
IT Human immunodeficiency virus 1
Sulfation
(HIV-1 Tat protein interaction with heparin: role of backbone structure, sulfation, and size)
IT Transcription factors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(tat; HIV-1 Tat protein interaction with heparin: role of backbone structure, sulfation, and size)
IT 9005-49-6, Heparin, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(HIV-1 Tat protein interaction with heparin: role of backbone structure, sulfation, and size)

L102 ANSWER 20 OF 31 HCAPLUS COPYRIGHT 2002 ACS
AN 1996:572317 HCAPLUS
DN 125:272673
TI N-acetylated domains in heparan sulfates revealed by a monoclonal antibody

against the Escherichia coli **K5** capsular **polysaccharide** . Distribution of the cognate epitope in normal human kidney and transplant kidney with chronic vascular rejection

AU van den Born, Jacob; Jann, Klaus; Assmann, Karel J. M.; Lindahl, Ulf; Berden, Jo H. M.
CS Div. Nephrol., Univ. Hosp. St. Radboud, Nijmegen, 6500 HB, Neth.

SO Journal of Biological Chemistry (1996), 271(37), 22802-22809
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
CC 14-12 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 9

AB The Escherichia coli **K5** capsular **polysaccharide** has the same (GlcUA .fwdarw. GlcNAc)n structure as the nonsulfated heparan sulfate/heparin precursor **polysaccharide**. A monoclonal antibody (mAb 865) against the **K5 polysaccharide** has been described (Peters, H., et al., 1985). In this report, we demonstrate the binding of anti-**K5** mAb 865 to N-acetylated sequences in heparan sulfates and heparan sulfate proteoglycans but not to heparin. This is shown by direct binding and fluid phase inhibition of mAb 865 in an ELISA. In this system we found that the binding of the mAb decreased with increasing sulfate content of the **polysaccharide**. By testing chem. modified **K5** and heparin **polysaccharides**, we found that each of the modifications that occur during heparan sulfate (HS) synthesis (N-sulfation, C-5 **epimerization**, and O-sulfation) prevents recognition by mAb 865. Samples of heparan sulfate from human aorta (HS-II) were selectively degraded so as to allow the sep. isolation of N-sulfated and N-acetylated block structures. N-Sulfated **oligosaccharides** (obtained after N-deacetylation by hydrazinolysis followed by nitrous acid deamination at pH 3.9) were not recognized by mAb 865, in contrast to N-acetylated **oligosaccharides** (obtained after nitrous acid deamination at pH 1.5), although the reactivity was lower than for intact HS-II. Anal. of the latter's pH 1.5 deamination products by gel filtration indicated that a minimal size of 18 **saccharide** units was necessary for antibody binding. These results lead us to propose bivalent antibody-heparan sulfate interaction, in which both F(ab) domains of the mAb interact with their epitopes, both of which are present in a single large (.gtoreq.18 **saccharide** units) N-acetylated domain and addnl. with single epitopes present in two N-acetylated sequences (each <18 **saccharide** units) bridged by a short N-sulfated domain. Immunohistochem. with mAb 865 on cryostat sections of normal human kidney tissue, revealed its binding to most but not all renal basement membranes. However, all renal basement membranes contain heparan sulfate, as shown by a mAb against heparitinase-digested heparan sulfate stubs (mAb 3G10). This finding indicates that not all heparan sulfate chains present in basement membranes express the mAb 865 epitopes. Besides the normal distribution, mAb 865 staining was found in fibrotic and sclerotic lesions in vessels, interstitium, and mesangium in transplant kidneys with chronic vascular rejection. Occasionally, a decrease of staining was obsd. within tubulo-interstitium and glomeruli. These findings show that N-acetylated sequences in heparan sulfates can be demonstrated by anti-**K5** mAb 865 in normal and diseased kidneys.

ST acetylation heparan sulfate monoclonal antibody; kidney disease transplant heparan sulfate acetylation

IT Kidney
(N-acetylated domains in heparan sulfates revealed by a monoclonal antibody and distribution in normal human kidney and transplant kidney with chronic vascular rejection)

IT Polysaccharides, biological studies
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)
(bacterial; N-acetylated domains in heparan sulfates revealed by a

monoclonal antibody to)

IT Antibodies
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(monoclonal, N-acetylated domains in heparan sulfates revealed by a monoclonal antibody and distribution in normal human kidney and transplant kidney with chronic vascular rejection)

IT Kidney
(transplant, N-acetylated domains in heparan sulfates revealed by a monoclonal antibody and distribution in normal human kidney and transplant kidney with chronic vascular rejection)

IT 9050-30-0, Heparan sulfate
RL: ANT (Analyte); BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(N-acetylated domains in heparan sulfates revealed by a monoclonal antibody and distribution in normal human kidney and transplant kidney with chronic vascular rejection)

L102 ANSWER 21 OF 31 HCAPLUS COPYRIGHT 2002 ACS
AN 1996:464356 HCAPLUS
DN 125:115073
TI Process for the preparation of iduronic acid-containing polysaccharides as anticoagulants and antithrombotics
IN **Zoppetti, Giorgio; Oreste, Pasqua;** Cipolletti, Giovanni
PA Inalco S.P.A., Italy
SO PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C12P019-26
ICS C07H005-04; A61K031-725
CC 33-8 (**Carbohydrates**)
Section cross-reference(s): 15
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9614425	A1	19960517	WO 1995-EP4241	19951030
W: AL, AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TM, TT, UA, UG, US, UZ, VN				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2204366	AA	19960517	CA 1995-2204366	19951030
AU 9539261	A1	19960531	AU 1995-39261	19951030
EP 789777	A1	19970820	EP 1995-937026	19951030
EP 789777	B1	20000809		
R: AT, CH, DE, DK, ES, FR, GB, IE, IT, LI, NL, PT, SE				
CN 1162339	A	19971015	CN 1995-196040	19951030
JP 10508204	T2	19980818	JP 1995-515019	19951030
AT 195348	E	20000815	AT 1995-937026	19951030
ES 2150589	T3	20001201	ES 1995-937026	19951030
US 5958899	A	19990928	US 1996-628690	19960412
PRAI IT 1994-MI2240	A	19941104		
WO 1995-EP4241	W	19951030		

AB Process for the prepn. of **polysaccharides** having a high iduronic acid content comprising: (a) N-deacetylation of the **polysaccharide K5** from E. coli or of the heparan sulfate or O-desulfation of heparin or heparan sulfate: (b) N-sulfation of the product obtained from the stage (a); (c) **epimerization** in presence of the C5 **epimerase** enzyme; (d) sulfation of at least some free hydroxy groups, wherein the stage (c) is carried out in a reaction medium

constituted by a classical buffer soln. formed by HEPES, potassium chloride, EDTA and TRITON X-100 to which a suitable additive is added.

ST E coli **polysaccharide K5 epimerization epimerase**; iduronic acid **polysaccharide** prepn anticoagulant

IT Polysaccharides, preparation
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(E. coli, iduronic acid-contg.; process for the prepn. of iduronic acid-contg. polysaccharides as anticoagulants and antithrombotics)

IT **Epimerization** and Anomerization
(enzymic; process for the prepn. of iduronic acid-contg. polysaccharides as anticoagulants and antithrombotics)

IT Uronic acids
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(polysaccharides; process for the prepn. of iduronic acid-contg. polysaccharides as anticoagulants and antithrombotics)

IT Anticoagulants and Antithrombotics
(process for the prepn. of iduronic acid-contg. polysaccharides as anticoagulants and antithrombotics)

IT **70766-66-4**
RL: CAT (Catalyst use); USES (Uses)
(process for the prepn. of iduronic acid-contg. polysaccharides as anticoagulants and antithrombotics)

IT 9005-49-6, Heparin, reactions 9050-30-0, Heparan sulfate
RL: RCT (Reactant); RACT (Reactant or reagent)
(process for the prepn. of iduronic acid-contg. polysaccharides as anticoagulants and antithrombotics)

IT **70766-66-4**
RL: CAT (Catalyst use); USES (Uses)
(process for the prepn. of iduronic acid-contg. polysaccharides as anticoagulants and antithrombotics)

RN 70766-66-4 HCAPLUS

CN Epimerase, polyglucuronate 5- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L102 ANSWER 22 OF 31 HCAPLUS COPYRIGHT 2002 ACS

AN 1996:334946 HCAPLUS

DN 125:87062

TI Biologically active, heparan sulfate-like species by combined chemical and enzymic modification of the Escherichia coli **polysaccharide K5**

AU Casu, Benito; Grazioli, Giordana; Hannesson, Helgi H.; Jann, Barbara; Jann, Klaus; Lindahl, Ulf; Naggi, Annamaria; **Oreste, Pasqua**; Razi, Nahid; et al.

CS Ist. Chim. Biochim. G. Ronzoni, Milan, Italy

SO Carbohydrate Letters (1994), 1(2), 107-114
CODEN: CLETEC; ISSN: 1073-5070

PB Harwood

DT Journal

LA English

CC 33-8 (**Carbohydrates**)
Section cross-reference(s): 7, 9, 15

AB Semi-synthetic heparan sulfate-like **glycosaminoglycans** have been prepd. from the E. coli **K5 polysaccharide**, by controlled N-deacetylation (with hydrazine), followed by N-sulfation (with trimethylamine.SO3), partial C-5-**epimeriazation** (with a purified

C-5 **epimerase**), and O-sulfation (with pyridine.SO3, and with a crude 3-O-sulfotransferase). The in vitro inhibition of activated Factor X by antithrombin of the end-products is similar to that of beef mucosal heparan sulfate.

ST **epimerization** sulfation heparan enzymic; uronate sulfate prepn factor x inhibition; heparan sulfate like prepn antithrombin

IT **Polysaccharides**, preparation
RL: PUR (Purification or recovery); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
(Escherichia coli, **K5**; prepn. of heparan sulfate-like by combined chem. and enzymic modification of the Escherichia coli **polysaccharide K5**)

IT **Epimerization** and Anomerization
Sulfation
(enzymic; prepn. of heparan sulfate-like by combined chem. and enzymic modification of the Escherichia coli **polysaccharide K5**)

IT Escherichia coli
(prepn. of heparan sulfate-like by combined chem. and enzymic modification of the Escherichia coli **polysaccharide K5**)

IT **37342-00-0, Epimerase**
RL: CAT (Catalyst use); USES (Uses)
(C-5; prepn. of heparan sulfate-like by combined chem. and enzymic modification of the Escherichia coli **polysaccharide K5**)

IT 73361-04-3P
RL: PUR (Purification or recovery); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
(Escherichia coli; prepn. of heparan sulfate-like by combined chem. and enzymic modification of the Escherichia coli **polysaccharide K5**)

IT 73361-04-3DP, sulfated
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation)
(prepn. of heparan sulfate-like by combined chem. and enzymic modification of the Escherichia coli **polysaccharide K5**)

IT **9000-94-6**, Antithrombin 9001-29-0, Factor X
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(prepn. of heparan sulfate-like by combined chem. and enzymic modification of the Escherichia coli **polysaccharide K5**)

IT **37342-00-0, Epimerase**
RL: CAT (Catalyst use); USES (Uses)
(C-5; prepn. of heparan sulfate-like by combined chem. and enzymic modification of the Escherichia coli **polysaccharide K5**)

RN 37342-00-0 HCAPLUS
CN Epimerase (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT **9000-94-6**, Antithrombin
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(prepn. of heparan sulfate-like by combined chem. and enzymic modification of the Escherichia coli **polysaccharide K5**)

RN 9000-94-6 HCAPLUS
CN Antithrombin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L102 ANSWER 23 OF 31 HCAPLUS COPYRIGHT 2002 ACS
AN **1995:446713** HCAPLUS
DN **122:196976**
TI Polysaccharides having high antithrombotic and anticoagulant activity
IN Casu, Benito; Grazioli, Giordana; Naggi, Annamaria; Torri, Giangiacomo; Lindahl, Ulf; Razi, Nahid; **Oreste, Pasqua**; Bossi, Maria Luisa
PA Italfarmaco S.p.A., Italy
SO PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C08B037-00
ICS C08B037-10; A61K031-725
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1, **44**
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9429352	A1	19941222	WO 1994-EP1660	19940524
	W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KG, KP, KR, KZ, LK, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ, VN				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9468448	A1	19950103	AU 1994-68448	19940524
	ZA 9403868	A	19950202	ZA 1994-3868	19940602
PRAI	IT 1993-MI1175		19930604		
	WO 1994-EP1660		19940524		

AB Polysaccharides consisting of chains or mixts. of chains having a mol. wt. ranging from about 1000 to about 100,000 Da, or more, said polysaccharides being characterized in that they have a repeating disaccharide sulfated at the N and O positions in varying percentages and the salts thereof with alkali or alk.-earth metal cations, have remarkable anticoagulant and antithrombic activities.
ST polysaccharide sulfate prepn anticoagulant antithrombotic
IT Anticoagulants and Antithrombotics
(polysaccharides having high antithrombotic and anticoagulant activity)
IT Polysaccharides, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(polysaccharides having high antithrombotic and anticoagulant activity)
IT 144046-10-6P 152324-79-3P, Heparosan
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(polysaccharides having high antithrombotic and anticoagulant activity)

L102 ANSWER 24 OF 31 HCAPLUS COPYRIGHT 2002 ACS
AN 1995:208089 HCAPLUS
DN 122:49818
TI Biosynthesis of heparin. XXV. Substrate specificities of glucosyltransferases involved in formation of heparin precursor and E. coli **K5** capsular **polysaccharides**
AU Lidholt, Kerstin; Fjelstad, Maria; Jann, Klaus; Lindahl, Ulf
CS Dep. Med. Physiol. Chem., Univ. Uppsala, Uppsala, Swed.
SO Carbohydrate Research (1994), 255, 87-101
CODEN: CRBRAT; ISSN: 0008-6215
DT Journal
LA English
CC 7-3 (Enzymes)

Section cross-reference(s): 33

AB The Escherichia coli **K5** capsular **polysaccharide** is composed of 4)GlcpA(.beta.1-4)GlcpNAc(.alpha.1-**disaccharide** units. A partially N-deacetylated/N-sulfated **heptasaccharide**, derived from this polymer and having a nonreducing terminal GlcNAc unit, was used as acceptor for a mastocytoma microsomal GlcA-transferase involved in heparin biosynthesis. An **octasaccharide** with nonreducing-terminal GlcA similarly served as acceptor for the microsomal GlcNAc-transferase. Anal. of the labeled octa- and nona-**saccharide** formed by transfer of **monosaccharide** units from UDP-[14C]GlcA and UDP-[3H]GlcNAc, resp., showed that both glycosyltransferases could utilize partially N-sulfated acceptors. The GlcA-transferase showed a marked preference for a terminal GlcNAc-GlcA-GlcNSO3-sequence, particularly when this sequence was followed by an addnl. N-sulfated **disaccharide** unit. Enzymes catalyzing the same GlcA and GlcNAc transfer reactions were solubilized from E. coli **K5** membranes. The **K5** capsular **polysaccharide**, like the heparin/heparan sulfate precursor **polysaccharide**, thus probably grows by stepwise, alternating addn. of the two constituent **monosaccharide** units, from the corresponding UDP-sugars, to the nonreducing ends of the chains. Moreover, the bacterial glycosyltransferases utilized the same partially N-sulfated **oligosaccharide** substrates as the mammalian enzymes, and with similar preference for N-sulfate groups in certain positions.

ST Escherichia glycosyltransferase heparin heparan sulfate formation

IT Molecular structure-biological activity relationship
(glucosyltransferase-substrate; substrate specificities of glucosyltransferases involved in formation of heparin precursor and E. coli **K5** capsular **polysaccharides**)

IT Escherichia coli
(substrate specificities of glucosyltransferases involved in formation of heparin precursor and E. coli **K5** capsular **polysaccharides**)

IT **Sulfation**
(biochem., substrate specificities of glucosyltransferases involved in formation of heparin precursor and E. coli **K5** capsular **polysaccharides**)

IT Mast cell
(neoplasm, substrate specificities of glucosyltransferases involved in formation of heparin precursor and E. coli **K5** capsular **polysaccharides**)

IT **Polysaccharides**, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); RCT (Reactant); BIOL (Biological study); PROC (Process); RACT (Reactant or reagent)
(sulfates, substrate specificities of glucosyltransferases involved in formation of heparin precursor and E. coli **K5** capsular **polysaccharides**)

IT 123425-54-7, Acetylglucosamine-**oligosaccharide** acetylglucosaminyltransferase 145539-84-0, UDPglucuronate-**oligosaccharide** glucuronosyltransferase
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(substrate specificities of glucosyltransferases involved in formation of heparin precursor and E. coli **K5** capsular **polysaccharides**)

IT 9005-49-6, Heparin, biological studies 9050-30-0, Heparan sulfate
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(substrate specificities of glucosyltransferases involved in formation of heparin precursor and E. coli **K5** capsular

polysaccharides)

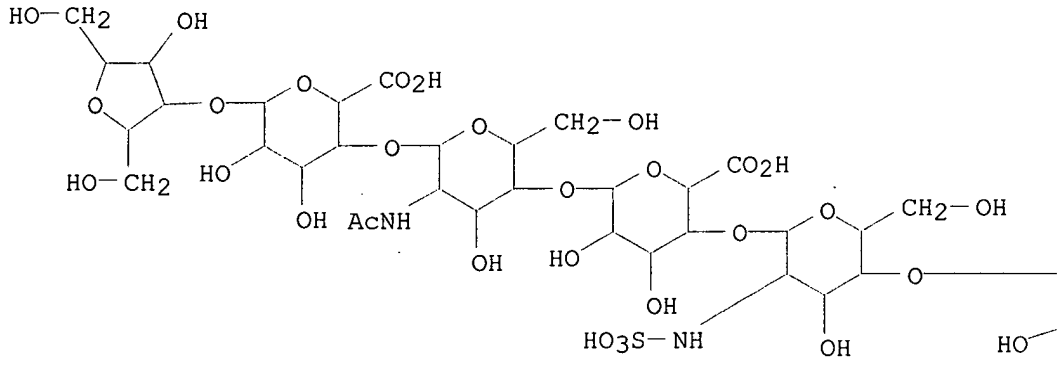
IT 158993-72-7 158993-73-8 **158993-74-9 158993-75-0 158993-76-1 158993-77-2 158993-78-3 158993-79-4** 158993-80-7 158993-81-8 158993-82-9 158993-83-0 158993-84-1 158993-85-2 158993-86-3 158993-87-4
RL: BPR (Biological process); BSU (Biological study, unclassified); RCT (Reactant); BIOL (Biological study); PROC (Process); RACT (Reactant or reagent)
(substrate specificities of glucosyltransferases involved in formation of heparin precursor and E. coli **K5** capsular **polysaccharides**)

IT **158993-74-9 158993-75-0 158993-76-1 158993-77-2 158993-78-3 158993-79-4**
RL: BPR (Biological process); BSU (Biological study, unclassified); RCT (Reactant); BIOL (Biological study); PROC (Process); RACT (Reactant or reagent)
(substrate specificities of glucosyltransferases involved in formation of heparin precursor and E. coli **K5** capsular **polysaccharides**)

RN 158993-74-9 HCAPLUS

CN D-Mannitol, O-2-(acetylamino)-2-deoxy-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.4)-O-2-deoxy-2-(sulfoamino)-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.4)-O-2-(acetylamino)-2-deoxy-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-2,5-anhydro- (9CI) (CA INDEX NAME)

PAGE 1-A



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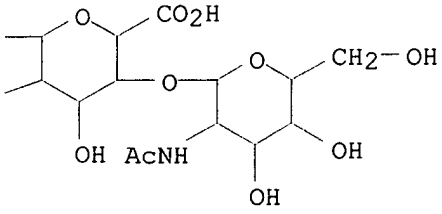
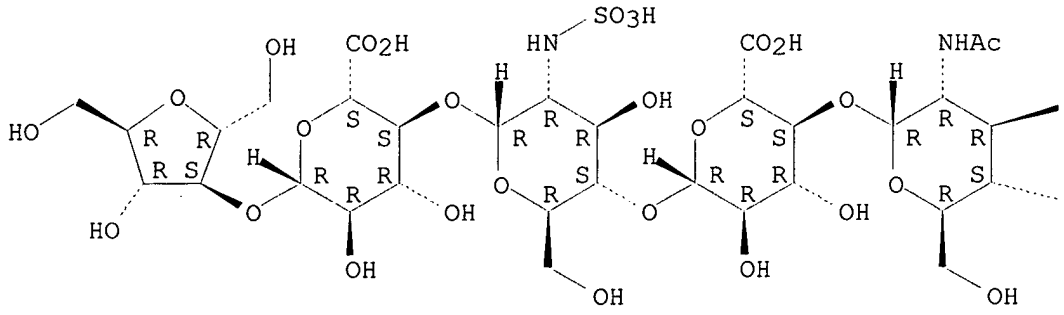


RN 158993-75-0 HCAPLUS
CN D-Mannitol, O-2-(acetylamino)-2-deoxy-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.4)-O-2-(acetylamino)-2-deoxy-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.4)-O-2-deoxy-2-(sulfoamino)-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-2,5-anhydro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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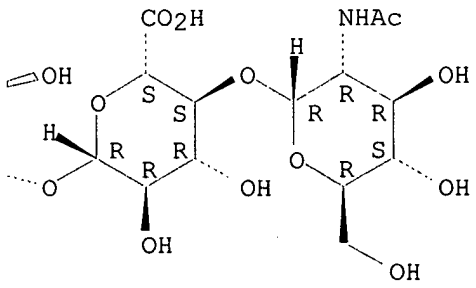

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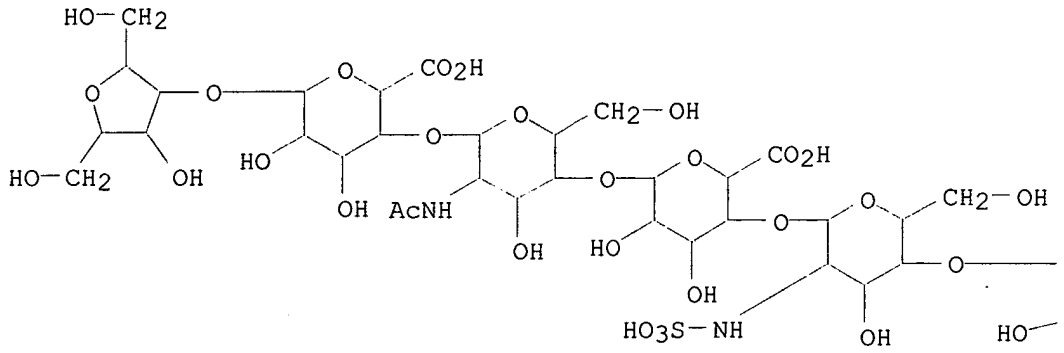
2-(acetylamino)-2-deoxy-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-2,5-anhydro- (9CI) (CA INDEX NAME)

PAGE 1-A



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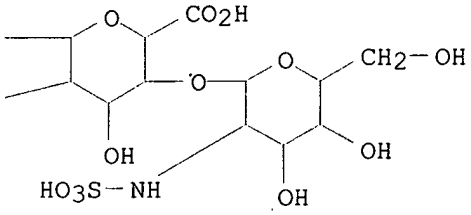

RN 158993-77-2 HCAPLUS

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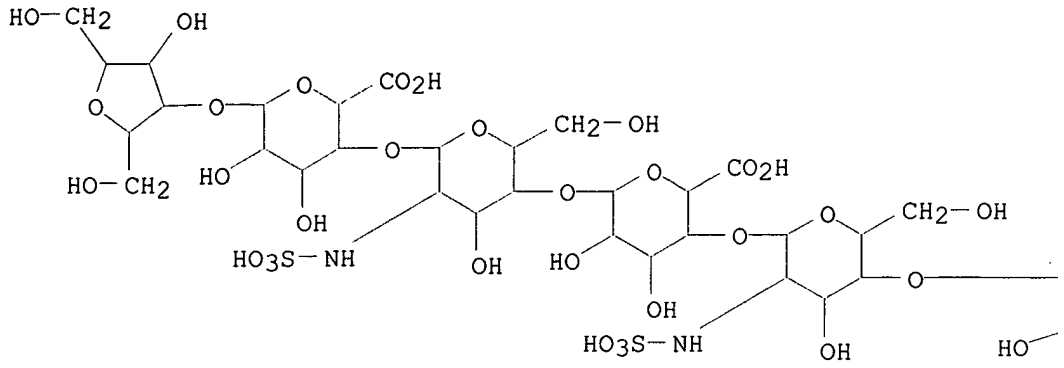
PAGE 1-A



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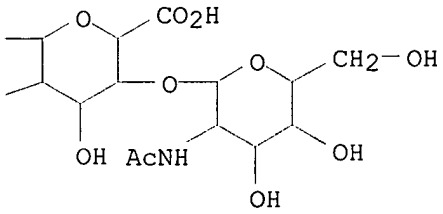

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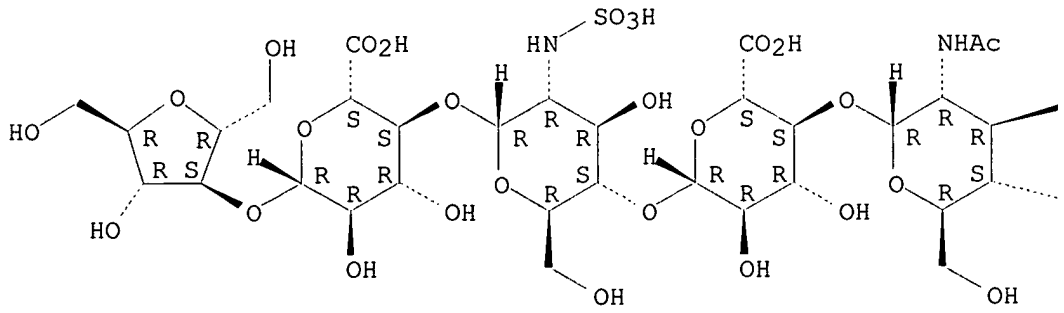
Absolute stereochemistry.

PAGE 1-A



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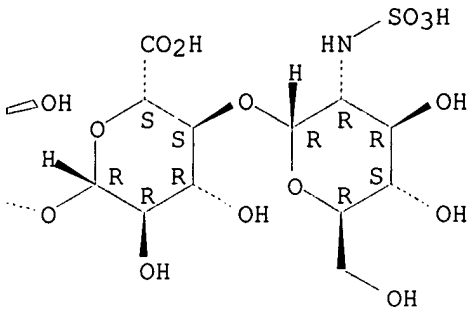
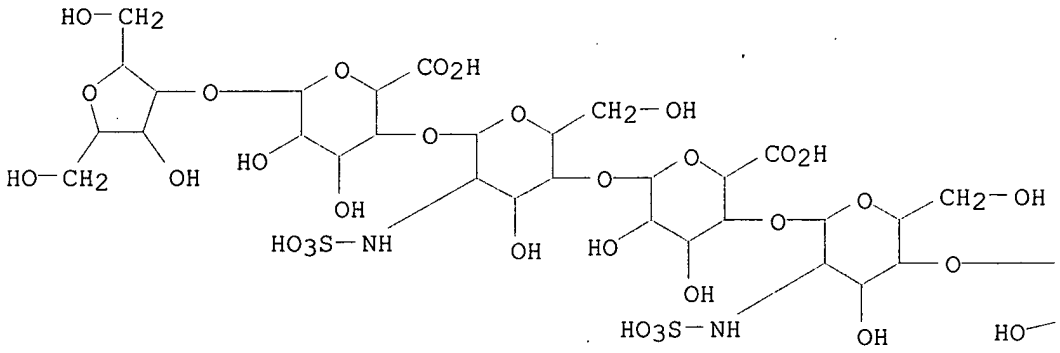


RN 158993-79-4 HCAPLUS
CN D-Mannitol, O-2-deoxy-2-(sulfoamino)-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.4)-O-2-deoxy-2-(sulfoamino)-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.4)-O-2-deoxy-2-(sulfoamino)-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-2,5-anhydro- (9CI) (CA INDEX NAME)

PAGE 1-A



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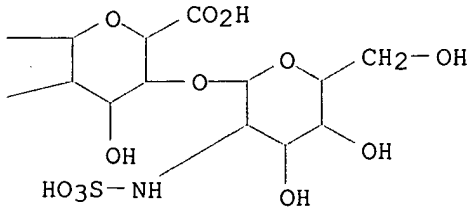


L102 ANSWER 25 OF 31 HCAPLUS COPYRIGHT 2002 ACS
AN 1995:140917 HCAPLUS
DN 123:33555
TI Heparin-like compounds prepared by chemical modification of capsular **polysaccharide** from E. coli **K5**
AU Casu, Benito; Grazioli, Giordana; Razi, Nahid; Guerrini, Marco; Naggi, Annamaria; Torri, Giangiacomo; **Oreste, Pasqua**; Tursi, Francesco; **Zoppetti, Giorgio**; et al.
CS Istituto di Chimica e Biochimica G. Ronzoni, Milan, Italy
SO Carbohydrate Research (1994), 263(2), 271-84
CODEN: CRBRAT; ISSN: 0008-6215
PB Elsevier
DT Journal
LA English
CC 33-8 (**Carbohydrates**)
Section cross-reference(s): 1
GI

—4-?-D-GlcA(1—4)-?-D-GlcNSO$_3^-$-(1— I

AB O-Sulfation of sulfaminoheparosan SAH, a glycosaminoglucuronan I, obtained by N-deacetylation and N-sulfation of the capsular **polysaccharide** from E. coli **K5**, was investigated in order to characterize the sulfation pattern eliciting heparin-like activities. SAH was reacted (as the tributylammonium salt in N, N-dimethylformamide) with pyridine-sulfur trioxide under systematically different exptl. conditions. The structure of O-sulfated products (SAHS), as detd. by mono- and two-dimensional 1H and 13C NMR, varied with variation of reaction parameters. Sulfation of SAH preferentially occurred at O-6 of the GlcNSO-3 residues. Further sulfation occurred either at O-3 or at O-2 of the GlcA residues, depending on the exptl. conditions. Products with significantly high affinity for antithrombin and anti-**factor Xa** activity were obtained under well-defined conditions. These products contained the trisulfated amino sugar GlcNSO-33,6SO-3, which is a marker component of the **pentasaccharide** sequence through which heparin binds to antithrombin.
ST antifactor activity heparin like; antithrombin binding heparin like; capsule polysaccharide coli sulfation; sulfaminoheparosan sulfation
IT **Sulfation**
(heparin-like compds. prepd. by chem. modification of capsular polysaccharide from E. coli)
IT **145213-57-6P 155732-42-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(heparin-like compds. prepd. by chem. modification of capsular polysaccharide from E. coli)
IT **155732-41-5P 164082-46-6P 164203-88-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(heparin-like compds. prepd. by chem. modification of capsular polysaccharide from E. coli)
IT **9000-94-6**, Antithrombin 78245-16-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(heparin-like compds. prepd. by chem. modification of capsular polysaccharide from E. coli)
IT 164082-45-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

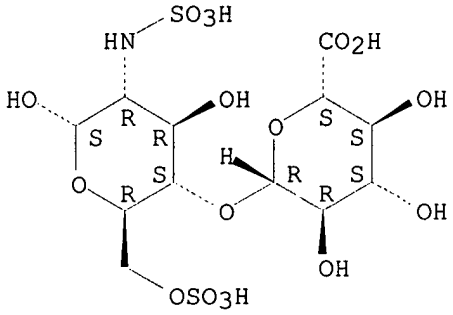
(Reactant or reagent)
(heparin-like compds. prepd. by chem. modification of capsular polysaccharide from E. coli)

IT **145178-41-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(heparin-like compds. prepd. by chem. modification of capsular polysaccharide from E. coli)

IT **145213-57-6P 155732-42-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(heparin-like compds. prepd. by chem. modification of capsular polysaccharide from E. coli)

RN 145213-57-6 HCAPLUS
CN .alpha.-D-Glucopyranose, 2-deoxy-4-O-.beta.-D-glucopyranuronosyl-2-(sulfoamino)-, 6-(hydrogen sulfate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 155732-42-6 HCAPLUS
CN .alpha.-D-Glucopyranose, 2-deoxy-4-O-.beta.-D-glucopyranuronosyl-2-(sulfoamino)- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

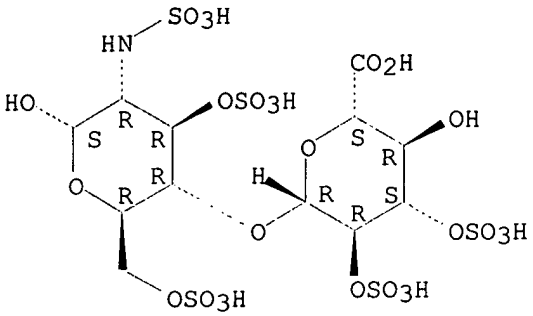
IT **155732-41-5P 164082-46-6P 164203-88-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(heparin-like compds. prepd. by chem. modification of capsular polysaccharide from E. coli)

RN 155732-41-5 HCAPLUS
CN .alpha.-D-Glucopyranose, 2-deoxy-2-(sulfoamino)-4-O-(2-O-sulfo-.beta.-D-glucopyranuronosyl)-, 6-(hydrogen sulfate) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

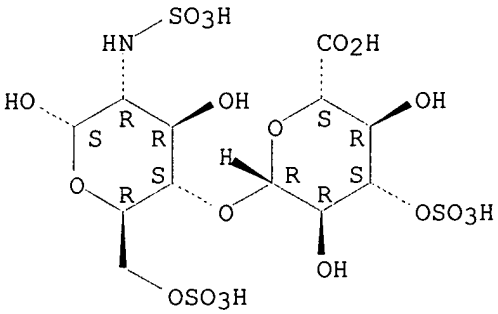
RN 164082-46-6 HCAPLUS
CN .alpha.-D-Glucopyranose, 2-deoxy-4-O-(2,3-di-O-sulfo-.beta.-D-glucopyranuronosyl)-2-(sulfoamino)-, 3,6-bis(hydrogen sulfate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 164203-88-7 HCAPLUS
CN .alpha.-D-Glucopyranose, 2-deoxy-2-(sulfoamino)-4-O-(3-O-sulfo-.beta.-D-glucopyranuronosyl)-, 6-(hydrogen sulfate) (9CI) (CA INDEX NAME)

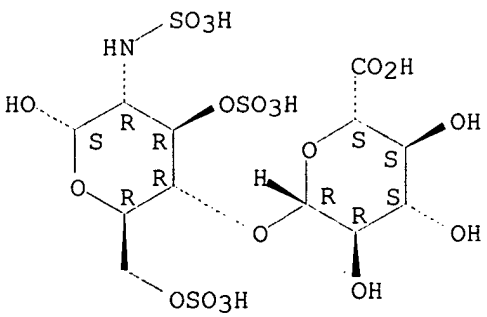
Absolute stereochemistry.



IT **9000-94-6**, Antithrombin
RL: RCT (Reactant); RACT (Reactant or reagent)
(heparin-like compds. prepd. by chem. modification of capsular polysaccharide from E. coli)
RN 9000-94-6 HCAPLUS
CN Antithrombin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **145178-41-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(heparin-like compds. prepd. by chem. modification of capsular polysaccharide from E. coli)
RN 145178-41-2 HCAPLUS
CN .alpha.-D-Glucopyranose, 2-deoxy-4-O-.beta.-D-glucopyranuronosyl-2-(sulfoamino)-, 3,6-bis(hydrogen sulfate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L102 ANSWER 26 OF 31 HCAPLUS COPYRIGHT 2002 ACS
AN 1994:624763 HCAPLUS
DN 121:224763
TI Biosynthesis of heparin/heparan sulfate. Purification of the D-**glucuronyl** C-5 **epimerase** from bovine liver
AU Campbell, Patrick; Hannesoson, Helgi H.; Sandbaeck, Dagmar; Roden, Lennart; Lindahl, Ulf; Li, Jin-ping
CS Univ. Alabama, Birmingham, AL, 35294, USA
SO Journal of Biological Chemistry (1994), 269(43), 26953-8
CODEN: JBCHA3; ISSN: 0021-9258
DT Journal
LA English
CC 7-2 (Enzymes)
AB The D-**glucuronyl** C-5 **epimerase** involved in the biosynthesis of heparin/heparan sulfate was purified from the high speed supernatant fraction of a homogenate of bovine liver by chromatog. on immobilized O-desulfate heparin, red Sepharose, Ph Sepharose, and Con A-Sepharose. After close to 1 million-fold purifn., 10-15% yield, the product gave a single band on SDS-PAGE with silver staining and had a mobility corresponding to an Mr of .apprx.52,000. Since the **epimerase** assay used in the course of purifn. was based on release of tritium, as [3H]H2O, from a [5-3H]uronyl-labeled substrate, it was important to establish that the purified enzyme did indeed catalyze the actual conversion of D-**glucuronyl** to L-**iduronyl** residues. Upon incubation of the purified enzyme with 3H-labeled heparosan N-sulfate, prepd. by metabolic labeling (with D-[1-3H]glucose) of a capsular **polysaccharide** from Escherichia coli **K5** and subsequent chem. partial N-deacetylation and N-sulfation, approx. 30% of the D-**glucuronyl** residues located between two N-sulfated glucosamine units were converted to L-**iduronyl** units.
ST **glucuronyl epimerase** liver
IT Liver
(purifn. and properties of **glucuronyl** C-5 **epimerase** from bovine liver)
IT Amino acids, biological studies
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(purifn. and properties of **glucuronyl** C-5 **epimerase** from bovine liver)
IT **112567-86-9**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(purifn. and properties of **glucuronyl** C-5 **epimerase** from bovine liver)
IT 9005-49-6, Heparin, biological studies 9050-30-0, Heparan sulfate
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(purifn. and properties of **glucuronyl** C-5 **epimerase** from bovine liver)
IT **112567-86-9**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(purifn. and properties of **glucuronyl** C-5 **epimerase** from bovine liver)
RN 112567-86-9 HCAPLUS
CN Epimerase, heparosan N-sulfate D-glucuronosyl 5- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L102 ANSWER 27 OF 31 HCAPLUS COPYRIGHT 2002 ACS
AN 1993:441829 HCAPLUS
DN 119:41829

TI Biochemical bases of the interaction of human basic fibroblast growth factor with **glycosaminoglycans**. New insights from trypsin digestion studies

AU Coltrini, Daniela; Rusnati, Marco; **Zoppetti, Giorgio; Oreste, Pasqua**; Isacchi, Antonella; Caccia, Paolo; Bergonzoni, Laura; Presta, Marco

CS Sch. Med., Univ. Bresica, Italy

SO European Journal of Biochemistry (1993), 214(1), 51-8
CODEN: EJBCAI; ISSN: 0014-2956

DT Journal

LA English

CC 2-10 (Mammalian Hormones)

AB In the present study the authors have attempted a characterization of the biochem. bases of the interaction of human basic fibroblast growth factor (bFGF) with **glycosaminoglycans** (GAGs) in soln. This interaction has been evidenced as the capacity of different GAGs and various sulfated compds. to protect bFGF and different bFGF mutants from tryptic cleavage. Heparin protects bFGF from trypsin digestion in a dose-dependent fashion. Substitution by site-directed mutagenesis of two or more basic residues with neutral glutamine residues in the amino-terminal region bFGF(27-32) or in the carboxyl-terminal region bFGF(118-129) does not significantly affect the protective effect exerted by heparin. In contrast, heparin protection is abolished when the full region bFGF(27-32) is deleted. The capacity of different GAGs to protect bFGF from proteolytic cleavage decreases in the following order: heparin > heparan sulfate > dermatan sulfate = chondroitin sulfates A and C > hyaluronic acid = **K5 polysaccharide**, indicating that both the degree of sulfation and the backbone structure of GAG modulate its interaction with bFGF. This is confirmed by the different capacity of various sulfated compds. (including dextran sulfates, suramin, trypan blue, and sulfate ion) to protect bFGF from tryptic digestion. Moreover, tryptic digestion studies performed with various heparin mols. and dextran sulfates of different size, ranging from 2.0 kDa to 500 kDa, indicate that the no. of bFGF mols. which interact with a single mol. of **polysaccharide** is related to the mol. mass of the GAG and that six hexose residues are sufficient to protect 1-2 mols. bFGF. In conclusion, the authors findings indicate that the capacity of GAGs to protect bFGF from tryptic cleavage depends upon their size, sulfation, distribution of the anionic sites along the chain, and structural requirements of the bFGF mol. These studies will help to design synthetic **oligosaccharides** endowed with different bFGF agonist and/or antagonist activities.

ST basic FGF proteolysis **glycosaminoglycan**

IT **Polysaccharides**, biological studies
RL: BIOL (Biological study)
(**K5**, basic FGF proteolysis prevention by, mechanism of)

IT **Glycosaminoglycans**, biological studies
RL: BIOL (Biological study)
(basic FGF proteolysis prevention by, mechanism of)

IT Molecular structure-biological activity relationship
(**glycosaminoglycan**-binding, of human basic fibroblast growth factor)

IT 9004-61-9, Hyaluronic acid 9005-49-6, Heparin, biological studies 9042-14-2, Dextran sulfate 9050-30-0, Heparan sulfate 24967-93-9, Chondroitin sulfate A 24967-94-0, Dermatan sulfate 25322-46-7, Chondroitin sulfate C
RL: BIOL (Biological study)
(basic FGF proteolysis prevention by, mechanism of)

IT 106096-93-9, Basic fibroblast growth factor
RL: BIOL (Biological study)
(proteolysis of, **glycosaminoglycans** prevention of, mechanism of)

L102 ANSWER 28 OF 31 HCAPLUS COPYRIGHT 2002 ACS

AN 1993:55633 HCAPLUS
DN 118:55633
TI Anticoagulants from Escherichia coli saccharide
IN Jann, Klaus; Jann, Barbara; Casu, Benito; Torri, Giangiacomo; Naggi, Annamaria; Grazioli, Giordana; Lindahl, Ulf; Hannesson, Helgi H.; Kusche, Marion; et al.
PA Italfarmaco S.p.A, Italy; Max Planck Institut fuer Immunobiologie
SO Brit. UK Pat. Appl., 57 pp.
CODEN: BAXXDU
DT Patent
LA English
IC ICM C08B037-00
ICS A61K031-715; A61K031-73; A61K031-735; C12P019-04
CC 9-14 (Biochemical Methods)
Section cross-reference(s): 1, 16
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	GB 2254083	A1	19920930	GB 1991-6757	19910328
	GB 2286193	A1	19950809	GB 1995-8157	19910328
	WO 9217507	A1	19921015	WO 1992-GB571	19920330
	W: AT, AU, BB, BG, BR, CA, CH, CS, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, PL, RO, RU, SD, SE, US				
	RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GN, GR, IT, LU, MC, ML, MR, NL, SE, SN, TD, TG				
	AU 9214308	A1	19921102	AU 1992-14308	19920330
	ZA 9202313	A	19930802	ZA 1992-2313	19920330
	EP 577665	A1	19940112	EP 1992-907206	19920330
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, SE				
	JP 07501684	T2	19950223	JP 1992-506945	19920330
	HU 67208	A2	19950228	HU 1993-2732	19920330
	NO 9303440	A	19931026	NO 1993-3440	19930927
PRAI	GB 1991-6757		19910328		
	WO 1992-GB571		19920330		

AB The anticoagulants are chem. and enzymically prepd. in large quantity from the **K-5 saccharide** (of heparin-type) of E. coli, by N-deacetylation, e.g. using hydrazine/hydrazine sulfate, and optionally, followed by N-sulfation and/or enzymic C5-**epimerization** (e.g. of D-**glucuronic** acid residue to L-**iduronic** acid residue), and O-sulfation.
ST anticoagulant Escherichia saccharide deriv; heparin Escherichia modification anticoagulant; glucosamine **glucuronic** Escherichia anticoagulant manuf; deacetylation **epimerization** sulfation **glucuronoglucosacetylamine** saccharide
IT Fermentation
(**K-5 glucuronoacetylglucosamine polysaccharide**, by Escherichia coli, chem. and enzymic modification in anticoagulant manuf. in relation to)
IT Escherichia coli
(**K-5 saccharide** of, chem. and enzymic modification of, for anticoagulants)
IT Anticoagulants and Antithrombotics
(deacetylated and N- and/or O-sulfated and **epimerized K-5 saccharide** of Escherichia coli for, prepn. of)
IT **Polysaccharides**, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(**glucuronoacetylglucosamine**-type, **K-5**, of Escherichia coli, N-deacetylation and N-sulfation and **epimerization** and/or O-sulfation of, in anticoagulant manuf.)
IT **Sulfation**
(N- and O-, of Escherichia coli **K-5 glucuronoacetylglucosamine polysaccharide** in

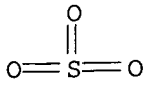
anticoagulant manuf.)
IT **Deacetylation**
(N-, of Escherichia coli **K-5 glucuronoacetylglucosamine polysaccharide** in anticoagulant manuf.)
IT **Epimerization** and Anomerization
(D-**glucuronyl**-L-**iduronyl**-C5-type, of Escherichia coli **K-5 glucuronoacetylglucosamine polysaccharide** in anticoagulant manuf.)
IT 10034-93-2, Hydrazine sulfate
RL: ANST (Analytical study)
(deacetylating agent, for transforming Escherichia coli **K-5 saccharide** in anticoagulant manuf.)
IT 302-01-2, Hydrazine, miscellaneous
RL: MSC (Miscellaneous)
(deacetylating agent, for transforming Escherichia coli **K-5 saccharide** in anticoagulant manuf.)
IT **42615-44-1**, K-5
RL: ANST (Analytical study)
(deacetylation and N-sulfation and **epimerization** and/or O-sulfation of, for anticoagulants)
IT **112567-86-9**
RL: RCT (Reactant); RACT (Reactant or reagent)
(**epimerization** by, in transforming Escherichia coli **K-5 saccharide** for anticoagulants)
IT 9023-09-0, Sulfotransferase
RL: ANST (Analytical study)
(for transforming Escherichia coli **K-5 saccharide** in anticoagulant manuf.)
IT **3162-58-1 26412-87-3**
RL: ANST (Analytical study)
(sulfating agent, for transforming Escherichia coli **K-5 saccharide** in anticoagulant manuf.)
IT **42615-44-1**, K-5
RL: ANST (Analytical study)
(deacetylation and N-sulfation and **epimerization** and/or O-sulfation of, for anticoagulants)
RN 42615-44-1 HCAPLUS
CN K 5 (polysaccharide) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **112567-86-9**
RL: RCT (Reactant); RACT (Reactant or reagent)
(**epimerization** by, in transforming Escherichia coli **K-5 saccharide** for anticoagulants)
RN 112567-86-9 HCAPLUS
CN Epimerase, heparosan N-sulfate D-glucuronosyl 5- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **3162-58-1 26412-87-3**
RL: ANST (Analytical study)
(sulfating agent, for transforming Escherichia coli **K-5 saccharide** in anticoagulant manuf.)
RN 3162-58-1 HCAPLUS
CN Methanamine, N,N-dimethyl-, compd. with sulfur trioxide (1:1) (9CI) (CA INDEX NAME)

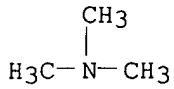
CM 1

CRN 7446-11-9
CMF O3 S



CM 2

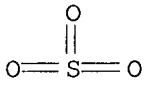
CRN 75-50-3
CMF C3 H9 N



RN 26412-87-3 HCAPLUS
CN Sulfur trioxide, compd. with pyridine (1:1) (9CI) (CA INDEX NAME)

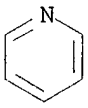
CM 1

CRN 7446-11-9
CMF O3 S



CM 2

CRN 110-86-1
CMF C5 H5 N



L102 ANSWER 29 OF 31 HCAPLUS COPYRIGHT 2002 ACS
AN 1991:201865 HCAPLUS
DN 114:201865
TI Biosynthesis of heparin. Use of Escherichia coli **K5** capsular **polysaccharide** as a model substrate in enzymic polymer-modification reactions
AU Kusche, Marion; Hannesson, Helgi H.; Lindahl, Ulf
CS Biomed. Cent., Swed. Univ. Agric. Sci., Uppsala, S-751 23, Swed.
SO Biochemical Journal (1991), 275(1), 151-8
CODEN: BIJOAK; ISSN: 0306-3275
DT Journal
LA English
CC 6-1 (General Biochemistry)
Section cross-reference(s): 7, 13
AB A capsular **polysaccharide** from E. coli **K5** has the same structure [-(4).beta.GlcA(1).fwdarw.(4).alpha.GlcNAc(1)-]n, as that of the nonsulfated precursor **polysaccharide** in heparin biosynthesis. The **K5 polysaccharide** was N-deacetylated (by

hydrazinolysis) and N-sulfated, and was then incubated with detergent-solubilized enzymes from a heparin-producing mouse mastocytoma, in the presence of adenosine 3'-phosphate 5'-phospho[35S]sulfate ([35S]PAPS). Structural anal. of the resulting 35S-labeled **polysaccharide** revealed the formation of all the major **disaccharide** units found in heparin. The identification of 2-O-[35S]sulfated IdoA (L-**iduronic** acid) as well as 6-O-[35S]sulfated GlcNSO3 units demonstrated that the modified **K5** **polysaccharide** served as a substrate in the hexuronosyl C-5-**epimerase** and the major O-sulfotransferase reactions involved in the biosynthesis of heparin. The GlcA units of the native (N-acetylated) E. coli **polysaccharide** were attacked by the **epimerase** only when PAPS was present in the incubations, whereas those of the chem. N-sulfated **polysaccharide** were **epimerized** also in the absence of PAPS, in accord with the notion that N-sulfate groups are required for **epimerization**. With increasing concns. of PAPS, the mono-O-sulfated **disaccharide** unit -IdoA(2-OSO3)-GlcNSO3- was progressively converted into the di-O-sulfated species -IdoA(2-OSO3)-GlcNSO3(6-OSO3)-. A small proportion of the 35S-labeled **polysaccharide** was found to bind with high affinity to the proteinase inhibitor antithrombin. This proportion increased with increasing concn. of PAPS up to a level corresponding to .apprx.1-2% of the total incorporated 35S. The solubilized enzymes thus catalyzed all the reactions required for the generation of functional antithrombin-binding sites.

ST heparin formation model **epimerization** sulfation; antithrombin heparin site formation; hexuronosyl C5 **epimerase** heparin formation; sulfotransferase heparin formation; capsular polysaccharide **epimerization** sulfation Escherichia

IT Microsome
(capsular polysaccharide deacetylated and sulfated form reaction with enzymes of, of mastocytoma, in heparin formation model)

IT Escherichia coli
(capsular polysaccharide of, deacetylation and sulfation and reactions with mastocytoma microsome enzymes of, as heparin formation model)

IT Molecular association
(of antithrombin with sulfate polysaccharide model of heparin)

IT **Deacetylation**
Sulfation
(of capsular polysaccharide, of Escherichia coli, in heparin formation model)

IT Mast cell
(neoplasm, capsular polysaccharide deacetylated and sulfated form reaction with microsome enzymes of, in heparin formation model)

IT Functional groups
(sulfate, essential, in **glucuronate** of polysaccharide reaction with hexuronosyl C-5 **epimerase** of mastocytoma microsome, in heparin formation model)

IT 57034-66-9 **112567-86-9**
RL: BIOL (Biological study)
(capsular polysaccharide deacetylated and sulfated form reaction with, of mastocytoma microsome, in heparin formation model)

IT 9005-49-6P, Heparin, biological studies
RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PREP (Preparation)
(formation of, Escherichia coli capsular polysaccharide deacetylated and sulfated form reactions with mastocytoma microsome enzymes as model for)

IT 482-67-7, Adenosine 3'-phosphate-5'-phosphosulfate
RL: BIOL (Biological study)
(**glucuronate** of capsular polysaccharide reaction with hexurinosyl C-5 **epimerase** of mastocytoma microsome requirement for, in heparin formation model)

IT **9000-94-6**, Antithrombin
RL: BIOL (Biological study)
(heparin binding site for, formation of, Escherichia coli capsular polysaccharide reactions with mastocytoma microsome enzymes in)
IT 6556-12-3, D-**Glucuronic** acid
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactions of, in polysaccharides, in heparin formation model with mastocytoma microsome enzymes)
IT 78245-16-6
RL: BIOL (Biological study)
(repeating unit, deacetylation and sulfation and reactions with mastocytoma microsome enzymes, as heparin formation model)
IT **112567-86-9**
RL: BIOL (Biological study)
(capsular polysaccharide deacetylated and sulfated form reaction with, of mastocytoma microsome, in heparin formation model)
RN 112567-86-9 HCAPLUS
CN Epimerase, heparosan N-sulfate D-glucuronosyl 5- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **9000-94-6**, Antithrombin
RL: BIOL (Biological study)
(heparin binding site for, formation of, Escherichia coli capsular polysaccharide reactions with mastocytoma microsome enzymes in)
RN 9000-94-6 HCAPLUS
CN Antithrombin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L102 ANSWER 30 OF 31 HCAPLUS COPYRIGHT 2002 ACS
AN 1984:611616 HCAPLUS
DN 101:211616
TI Synthesis of heparin fragments. A chemical synthesis of the trisaccharide O-(2-deoxy-2-sulfamido-3,6-di-O-sulfo-.alpha.-D-glucopyranosyl)-(1 .fwdarw. 4)-O-(2-O-sulfo-.alpha.-L-idopyranosyluronic acid)-(1 .fwdarw. 4)-2-deoxy-2-sulfamido-6-O-sulfo-D-glucopyranose heptasodium salt
AU Jacquinet, Jean Claude; Pettitou, Maurice; Duchaussoy, Philippe; Lederman, Isidore; Choay, Jean; Torri, Giangiacomo; Sinay, Pierre
CS Lab. Biochim. Structurale, ERA, Orleans, 45046, Fr.
SO Carbohydrate Research (1984), 130, 221-41
CODEN: CRBRAT; ISSN: 0008-6215
DT Journal
LA English
CC 33-8 (Carbohydrates)
AB Known 3-O-benzyl-1,2-O isopropylidene-.alpha.-D-glucofuranose was first converted into Me 3-O-benzyl-1,2-O-isopropylidene-.beta.-L-idofuranuronate. Acid hydrolysis, followed by acetylation and treatment with TiBr4, gave Me (2,4-di-O-acetyl-3-O-benzyl-.alpha.-L-idopyranosyl bromide)uronate, which was immediately transformed into Me 4-O-acetyl-3-O-benzyl-.beta.-L-idopyranuronate 1,2-(tert-Bu orthoacetate). A two-step replacement of the 4-O-acetyl by a 4-O-chloroacetyl group gave the key deriv., cryst. Me 3-O-benzyl-4-O-chloroacetyl-.beta.-L-idopyranuronate 1,2-(tert-Bu orthoacetate). Condensation of this orthoester with an excess of cryst. benzyl 6-O-acetyl-3-O-benzyl-2-(benzyloxycarbonyl)amino-2-deoxy-.alpha.-D-glucopyranoside in PhCl in the presence of 2,6-dimethylpyridinium perchlorate gave cryst. benzyl 6-O-acetyl-3-O-benzyl-2-(benzyloxycarbonyl)amino-2-deoxy-4-O-(Me 2-O-acetyl-3-O-benzyl-4-O-chloroacetyl-.alpha.-L-idopyranosyluronate)-.alpha.-D-glucopyranoside in 40% yield. O-Demonochloroacetylation, followed by condensation with 3,6-di-O-acetyl-2-azido-4-O-benzyl-2-deoxy-.alpha.-D-glucopyranosyl bromide in CH2Cl2 in the presence of 2,4,6-trimethylpyridine, Ag triflate, and mol. sieve provided benzyl O-(3,6-di-O-acetyl-2-azido-4-O-benzyl-2-deoxy-.alpha.-D-glucopyranosyl)-

(1.fwdarw.4)-O-(Me 2-O-acetyl-3-O-benzyl-.alpha.-L-idopyranosyluronate)-(1.fwdarw.4)-6-O-acetyl-3-O-benzyl-2-(benzyloxycarbonyl)amino-2-deoxy-.alpha.-D-glucopyranoside in 88% yield. O-Deacetylation with NaOH, followed successively by O-sulfation in DMF in the presence of SO3-Me3N complex, catalytic hydrogenolysis, and N-sulfation in water with the same sulfating agent, gave the title compd. This trisaccharide, which is a fragment of the minimal **antithrombin III**-binding region in heparin, neither binds to **antithrombin III** nor induces anti-Xa activity.

ST heparin fragment synthesis; trisaccharide heparin fragment synthesis; glycosaminoglycuronan fragment synthesis

IT Mucopolysaccharides, preparation
RL: PREP (Preparation)
(sulfated, synthesis of heparin **antithrombin III** -binding region trisaccharide)

IT Oligosaccharides
RL: RCT (Reactant); RACT (Reactant or reagent)
(tri-, synthesis of, of heparin **antithrombin III** -binding region)

IT 26922-15-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(acetylation of)

IT 93000-10-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(benzylation of)

IT 92955-17-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and acetylation of)

IT 87907-35-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and benzoylation of)

IT 87326-79-2P 87326-80-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and bromination of)

IT 92955-27-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and catalytic hydrogenolysis and N-sulfation of)

IT 87327-03-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and conversion of, to orthoacetate deriv.)

IT 87326-81-6P 87326-82-7P 87907-39-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and deacetylation of)

IT 93000-11-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and debenzylidenation of)

IT 87907-10-6P 92955-25-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and dechloroacetylation of)

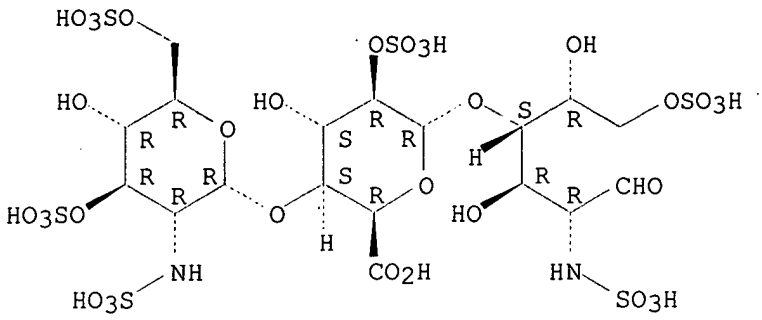
IT 87326-76-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and deisopropylidenation of)

IT 87326-73-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and **epimerization** of)

IT 92955-34-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. and oxidn. of)
IT 87907-36-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction of, with Me benzylidopyranuronate orthoacetate deriv.)
IT 87907-06-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction of, with Me idopyranuronate orthoacetate deriv.)
IT 87907-11-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction of, with azidodeoxyglucopyranosyl bromide deriv.)
IT 87907-09-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reactions of)
IT 87907-40-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and sulfation of)
IT 87326-83-8P 92955-20-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and trichloroacetylation of)
IT 87326-85-0P 87326-86-1P 87326-99-6P 87327-00-2P 92955-18-5P
92955-19-6P 92955-21-0P 92955-22-1P 92955-23-2P 92955-24-3P
92955-26-5P **92955-28-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
IT 67546-24-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with benzyl (Me idopyranosyluronate)glucopyranoside deriv.)
IT 9005-49-6DP, **antithrombin III**-binding region trisaccharide
RL: RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of)
IT 22529-61-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(tritylation and acetylation of)
IT **92955-28-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 92955-28-7 HCAPLUS
CN D-Glucose, O-2-deoxy-3,6-di-O-sulfo-2-(sulfoamino)-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-2-O-sulfo-.alpha.-L-idopyranuronosyl-(1.fwdarw.4)-2-deoxy-2-(sulfoamino)-, 6-(hydrogen sulfate), heptasodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.



●7 Na

L102 ANSWER 31 OF 31 HCAPLUS COPYRIGHT 2002 ACS
AN **1981:71278** HCAPLUS
DN **94:71278**
TI **Glycosaminoglycans** from pig duodenum
AU Casu, B.; Moretti, M.; **Oreste, P.**; Riva, A.; Torri, G.; Vercellotti, J. R.
CS Inst. Chim. Biochim. "G. Ronzoni", Milan, Italy
SO Arzneimittel-Forschung (1980), 30(11), 1889-92
CODEN: ARZNAD; ISSN: 0004-4172
DT Journal
LA English
CC 63-3 (Pharmaceuticals)
Section cross-reference(s): **33**
AB A polysaccharide ext. from pig duodenum, used in therapy as antilipemic, was shown by chromatog. and electrophoretic methods to be a mixt. of the **glycosaminoglycans** (GAG), heparin [9005-49-6], heparan sulfate [9050-30-0] dermatan sulfate (DeS) [24967-94-0], chondroitin sulfate [9007-28-7] and hyaluronic acid [9004-61-9], in the ratio 24:31:23:9:13. The GAG mixt. was fractionated with alkylammonium salts, and, for DeS, with Cu salts. Further purifn. of these fractions either by repeated complexation or by removal of residual impurities using sp. enzymes of chem. reactions., permitted obtaining individual GAG >97% pure by electrophoretic and 1H-NMR anal. These prepns. will be used to assess the contribution of individual GAG to the biol. activity of duodenal GAG exts.
ST **glycosaminoglycan** duodenum pig
IT Swine
(**glycosaminoglycans** from duodenum of)
IT Anticoagulants
(**glycosaminoglycans** from pig duodenum as)
IT Intestine
(duodenum, **glycosaminoglycans** from pig)
IT Mucopolysaccharides, biological studies
RL: BIOL (Biological study)
(**glycosaminoglycans**, from swine duodenum)
IT 9004-61-9 9005-49-6, biological studies 9007-28-7 9050-30-0 24967-94-0
RL: BIOL (Biological study)
(**glycosaminoglycans** from pig duodenum contg.)

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=> d all abeq tech abex tot

L116 ANSWER 1 OF 9 WPIX (C) 2002 THOMSON DERWENT
AN 2002-583547 [62] WPIX
CR 2001-656912 [75]
DNC C2002-164969
TI Preparation of **K5** glycosaminoglycans useful in the treatment of thrombosis involves N-deacetylation/N-sulfation of the polysaccharide, epimerization, oversulfation, O-desulfation and N-sulfation.
DC B03 B04
IN **ORESTE, P; ZOPPETTI, G**
PA (ORES-I) ORESTE P; (ZOPP-I) ZOPPETTI G
CYC 100
PI WO 2002050125 A2 20020627 (200262)* EN 50p C08B037-00 <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW
AU 2002022358 A 20020701 (200264) C08B037-00 <--
ADT WO 2002050125 A2 WO 2001-IB2492 20011217; AU 2002022358 A AU 2002-22358 20011217
FDT AU 2002022358 A Based on WO 200250125
PRAI US 2001-950003 20010912; US 2000-738879 20001218
IC ICM **C08B037-00**
AB WO 200250125 A UPAB: 20021031
NOVELTY - Preparation of **K5** glycosaminoglycans (III) involves N-deacetylation/N-sulfation of the polysaccharide **K5**, partial C5-epimerization of the carboxyl group of the glucuronic acid to the iduronic acid, oversulfation, selective O-desulfation, optional 6-O-sulfation, and N-sulfation.
DETAILED DESCRIPTION - Preparation of **K5** glycosaminoglycans (III) involves:
(a) N-deacetylation/N-sulfation of the polysaccharide **K5**;
(b) partial C5-epimerization of the carboxyl group of the glucuronic acid to the iduronic acid;
(c) oversulfation;
(d) selective O-desulfation;
(e) optional 6-O-sulfation; and
(f) N-sulfation.

The step (iv) involves treating the oversulfated product obtained in the step (iii) with a mixture of methanol/dimethyl sulfoxide for 135 - 165 (preferably 150) minutes at 60 deg. C.

INDEPENDENT CLAIMS are also included for the following:

(1) a C5-epimerized N,O-sulfate **K5** glycosaminoglycan prepared by:

(a) reacting polysaccharide **K5** with a N-deacetylating agent, then treating the N-deacetylated product with N-sulfating agent,

(b) submitting the **K5**-N-sulfate thus obtained to a C5-epimerization by glucuronosyl C5 epimerase to obtain a C5-epimerized N-sulfate **K5** in which the iduronic/glucuronic ratio is 60 plus or minus 40 - 40 plus or minus 60;

(c) converting the C5-epimerized N-sulfate **K5**, having a content of 40 - 60% iduronic acid over the total uronic acid, into a its tertiary or quaternary salt, then treating the salt thus obtained with an O-sulfating agent in an aprotic polar solvent at 40 - 60 deg. C for 10 - 20 hours;

(d) treating the salt with an organic base of the O-oversulfated product thus obtained with a mixture dimethyl sulfoxide/methanol at 50 - 70 deg. C for 135 - 165 minutes;

(e) treating a salt with an organic base of the partially O-desulfated product thus obtained with an O-sulfating agent at 0 - 5 deg. C; and

(f) treating the product thus obtained with a N-sulfating agent. The sodium salt of the end product is optionally converted into another salt;

(2) a pharmaceutical composition comprising (I) as an active ingredient and a carrier; and

(3) a glycosaminoglycan derived from **K5** polysaccharide constituted by a mixture of chains in which at least 80 (preferably at least 90)% of the chains having formula (I);

n = 3 - 100 (preferably 20 - 100);

R and R1 - R3 = H or SO3-.

Provided that :40 - 60 (preferably 55)% of uronic acid units is of iduronic acid. When about 50 - 65% of R, R1 - R3 are H, then the remaining is SO3, the group is distributed as follows: R3 is (85 - 95, preferably 85 - 90, especially 85)% SO3-, R2 is (17 - 21, preferably 20)% SO3-, R1 is (15 - 35, preferably 25)% SO3 in iduronic unit and 0 - 5% SO3- in glucuronic unit, R is (20 - 40) (preferably 30 - 35, especially 30)% SO3- in glucuronic unit and 0 - 5% in iduronic unit. The sum of the SO3- percent in R1, glucuronic units and in R1 iduronic units is 3 - 7 (preferably 5)%. Provided that R1 and R are not SO3- at the same time and are both H in 25 - 45 (preferably 30 - 40, especially 40) % of the uronic acid units. The sulfation degree is 2.3 - 2.9 (preferably 2.4 - 2.7, especially 2.55) and the corresponding cation is a chemically or pharmaceutically acceptable one.

ACTIVITY - Thrombolytic; Anticoagulant.

Test details are described but no results are given.

MECHANISM OF ACTION - None given.

USE - The **K5** glycosaminoglycans are useful in controlling coagulation in mammal (during surgical operations), for preventing or treating thrombosis in a mammal (claimed) and treating haematomas.

ADVANTAGE - (I) has high affinity for antithrombin III (ATIII) and high anticoagulant and antithrombotic activity. (I) shows bleeding potential lower than that of any other heparin-like glycosaminoglycan.

Dwg.0/10

FS CPI

FA AB; GI; DCN

MC CPI: B04-C02; B11-C01; B14-F04

TECH UPTX: 20020926

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Process: (III) can also be prepared by steps (a) - (f). The product obtained at the end of step (b) - (f) is optionally submitted to depolymerization. The C5 epimerization is performed using the enzyme glucuronosyl C5 epimerase in

solution or in immobilized form in presence of divalent cations. The C5 epimerization with enzyme in its immobilized form includes recirculating 20 - 1000 ml of a solution of Hepes (25 mM) at pH 6 - 7.4 (preferably 7) containing N-sulfated **K5** (0.002 - 10 g) and one of the cations at a concentration of 10 - 60 mM through a column containing 1.2x107 - 3x1011 cpm of the immobilized enzyme on an inert support. The C5 epimerization is performed with a recombinant enzyme at 30 degrees C by recirculating the solution with a flow rate of 200 ml/hour for 24 hours. In the step (c) the pyridine.sulfur trioxide is used as O-sulfating agent. In the step (d) the reaction is carried out in dimethyl sulfoxide/methanol 9+/-1 (vol./vol.) at 60 degrees C for 150 minutes. In the step (e), the 6-O-sulfation is carried out at 0 - 5 degrees C using pyridine.sulfur trioxide adduct as O-sulfating agent. The product obtained at the end of step (f) is submitted to a nitrous acid depolymerization followed by a reduction by sodium borohydride. (I) is isolated in the form of its sodium salt, which is further converted into another salt.
Preferred Components: The **K5** used, as the starting material is a previously purified **K5**. The N-deacetylating agent used in step (a) is hydrazine or its salt or an alkaline metal hydroxide and the N-sulfating agent is pyridine.sulfur trioxide or trimethylamine.sulfur trioxide adducts. The divalent cation comprises at least one of Ba, Ca, Mg or Mn. The epimerase in step (b) comprises recombinant lucuronosyl C5 epimerase, glucuronosyl C5 epimerase from murine mastocytoma and glucuronosyl C5 epimerase extracted from bovine liver. The other salt is another alkaline metal or alkaline earth metals, ammonium, 1-4C trialkylammonium, aluminum or zinc salt. The corresponding cation is alkaline metal, alkaline earth metal, aluminum or zinc ion (preferably sodium or calcium ion). The chains in the mixture of chains has molecular weight distribution of 2000 - 100000 (preferably 9000 - 60000) with a mean molecular weight of 4000 - 8000 (preferably 6000 - 8000, especially 7000, particularly 7400) or 12000 - 30000 (preferably 14000 - 16000, especially 15700).

ABEX

WIDER DISCLOSURE - Compounds of formula (I) are disclosed as new.

ADMINISTRATION - The composition contains 5 - 100 mg of (I) (claimed). The composition containing the compound is administered intravenously, subcutaneously or topically.
EXAMPLE - A K5 polysaccharide (10 g) obtained by fermentation as in MI99A001465 with purity of 80% was dissolved in deionized water to obtain 1% solution. Triton X-100 was added and the solution was kept at 55 degrees C for 2 hours under stirring. The solution was brought to 75 degrees C and kept to this temperature. The aqueous phase containing K5 was concentrated and precipitated with acetone or ethanol. The product obtained was 90% pure K5.
The previously purified K5 was dissolved in 2M sodium hydroxide (1000 ml) and kept at 60degreesC for 18 hours. The solution was cooled to room temperature to form N-deacetylated K5 (A) product. The solution containing (A) was kept at 40degreesC and added with sodium carbonate (10 g) in one step and adduct pyridine.sulfur trioxide (20 g) in 10 minutes. The product obtained N-sulfate K5 (B) was purified by diafiltration. The product formed was concentrated to 10% polysaccharide. A recombinant C5 epimerase (5 mg) was dissolved in 25 mM Hepes buffer (200 ml, pH 7.4) containing 0.1M KCl, 0.1% Triton X-100 and 15 mM ethylenediaminotetraacetic acid (EDTA).
(B) (100 mg) was then added. To a diafiltrated solution, after concentration to 50 ml, CNBr activated Sepharose 4B resin (50 ml) was added and kept to react overnight to 4 degrees C. To measure the activity of the immobilized enzyme an immobilized enzyme theoretically correspondent to 1.2x107 cpm was loaded. In the column, (B) was dissolved in 25 mM Hepes, 0.1M KCl, 0.015M EDTA, 0.01% Triton X-100 buffer was dissolved, recirculated in the column at 37 degrees C. After purification the ratio of iduronic acid/glucuronic acid was 30/70. (B) (10 g) was

dissolved in 25 mM Hepes buffer (600 ml) containing CaCl2 (50 mM). The solution was recirculated through a column. The reaction was performed at 30 degrees C with a flow rate of 200 ml/hour for 24 hours. The epimerized product had iduronic acid/glucuronic acid ratio of 54+/-46 against a ratio of 0+/-100 of the starting material. The epimerized product was cooled to 10 degrees C and applied to a cationic exchange resin. Both the column and the container were kept at 10 degrees C. The acidic solution was made neutral using tetrabutylammonium hydroxide. The product was suspended in dimethylformamide (200 ml) and added with adduct pyridine.SO3 (150 g) dissolved in DMF (200 ml). The solution was cooled to room temperature and added with acetone saturated with sodium chloride (1200 ml). The pellets obtained were separated by filtration, dissolved with deionized water (100 ml) and sodium chloride was added. the pellets were separated by filtration. The product (E) was solubilized with deionized water (100 ml) and purified by diafiltration.
The solution containing (E) was passed through cationic exchange resin. The solution was concentrated at 40degreesC and freeze-dried. The product obtained as pyridine salt was added to a solution of DMSO/methanol and the solution was kept at 60degreesC for 2.5 hours. The product (E1) was purified by diafiltration. The solution containing (E1) was passed through cationic exchange resin and was washed with water. The solution was concentrated and freeze-dried. The product, tetrabutylammonium salt was suspended in DMF (200 ml). The suspension was cooled to 0 degrees C and treated with adduct pyridine.SO3 (40 g) dissolved in DMF (100 ml). The sulfating agent was added in one step and the solution was kept at 0 degrees C for 1.5 hours and treated with acetone (750 ml) saturated with sodium chloride. The solution of the product obtained was treated for N-sulfation.
The glycosaminglycan compound (D) obtained by the process showed a mean molecular weight of 15700, sulfate/carboxyl ratio of 2.55, iduronic acid content of 54%, N-sulfate content of greater than 90%, 6-O sulfate content of 85%, 3-O sulfate glucosamine content of 20%, iduronic acid 2-O-sulfate content of 25%, glucuronic acid 3-O-sulfate content of 30%, no O-disulfate uronic unit, unsulfated uronic unit content of 40%. (D) showed 55% ATIII high affinity fraction and following in vitro anticoagulant activities as compared with the standard heparin taken as 100: anti-Xa 157, aPTT 78, anti-IIa 373, HCII 161.

DEFINITIONS - Preferred Definitions:
n = 3 - 15.

L116 ANSWER 2 OF 9 WPIX (C) 2002 THOMSON DERWENT
AN 2001-656912 [75] WPIX
CR 2002-583547 [62]
DNC C2001-193268
TI New N-deacetylated, N-sulfated derivatives of **K5** polysaccharide, useful as anticoagulant and antithrombotic agent, includes L-iduronic acid residues formed by epimerization.
DC A96 B04 D16
IN **ORESTE, P; ZOPPETTI, G**; CIPOLLETTI, G
PA (INAL-N) INALCO SPA; (ORES-I) ORESTE P; (ZOPP-I) ZOPPETTI G
CYC 95
PI WO 2001072848 A1 20011004 (200175)* EN 38p C08B037-10 <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001046510 A 20011008 (200208) C08B037-10 <--
US 2002062019 A1 20020523 (200239) C12P019-04
ADT WO 2001072848 A1 WO 2001-EP3461 20010327; AU 2001046510 A AU 2001-46510 20010327; US 2002062019 A1 CIP of US 2000-738879 20001218, US 2001-950003

20010912
FDT AU 2001046510 A Based on WO 200172848
PRAI IT 2000-MI665 20000330
IC ICM **C08B037-10**; C12P019-04
ICS A61K031-715; **C08B037-00**
AB WO 200172848 A UPAB: 20021001
NOVELTY - N-deacetylated, N-sulfated derivative (I) of **K5** polysaccharide that:
(a) is epimerized to at least 40% L-iduronic acid content (based on total uronic acids);
(b) has molecular weight 2-30 kD;
(c) contains 25-50 wt.% chains with high affinity for ATIII (antithrombin III); and
(d) has anticoagulant and antithrombotic activities characterized by HCII (heparin cofactor II) to anti-Xa ratio 1.5-4, is new.
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for preparing (I).
ACTIVITY - Anticoagulant; antithrombotic.
MECHANISM OF ACTION - Inhibition of thrombin. **K5** polysaccharide (80% pure; 10 g) was purified by heat treatment and precipitation, then incubated for 18 hours at 60 deg. C in 2N sodium hydroxide for N-deacetylation and reacted with pyridine-sulfur trioxide complex (A) at 40 deg. C for N-sulfation. The product, as a desalted 10% solution, was dissolved in 25 mM Hepes buffer (pH 6.5) containing 50 mM calcium chloride (600 ml) and circulated, for 24 hours and at 200 ml/hour and 37 deg. C, through a column of immobilized glucuronosyl C-5 epimerase. The product has iduronic acid:glucuronic acid ratio 48:52. This was converted to its tetrabutylammonium (TBA) salt and supersulfated using (A). The product was converted to pyridine salt and treated with dimethylsulfoxide and methanol for selective 6-sulfation and then (after conversion back to TBA salt) with (A) for N-sulfation. The final product had, relative to UF heparin as 100%, 76.6% anti-Xa activity; 43.4% activated prothrombin time; 256% heparin cofactor II activity and 118% anti-IIa activity. Its antithrombin III affinity was 29%, compared to 32% for heparin, i.e. reduced overall anticoagulant activity but greater thrombin inhibition.
USE - (I) is useful as anticoagulant and antithrombotic agent.
ADVANTAGE - (I) has high anticoagulant and antithrombotic activities and fewer side effects (especially bleeding) than heparin.
Dwg.0/11
FS CPI
FA AB; DCN
MC CPI: A03-A00A; A10-E01; A12-V01; B04-C02F; B14-F04; D05-A02; D05-C08
TECH UPTX: 20011220
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Material: (I) has molecular weight 4-8 or 18-30 kilo Dalton (kD).
Preparation: **K5** polysaccharide is isolated from Escherichia coli then:
(i) N-deacetylated (treatment with sodium hydroxide) and N-sulfated (e.g. reaction with pyridine-sulfur trioxide complex (A));
(ii) subjected to C5 epimerization of D-glucuronic acid residues to L-iduronic acid;
(iii) supersulfation (e.g. with (A));
(iv) selective O-desulfation (with dimethylsulfoxide and methanol); and
(v) selective 6-O-sulfation and N-sulfation (by treating a quaternary ammonium derivative with (A)).
Optionally the final product is fractionated according to molecular weight, e.g. by column chromatography or ultrafiltration. Step (ii) is with a glucuronosyl C-5 epimerase (B), in solution or immobilized, in presence of specific divalent cations (at least one of barium, calcium, magnesium and/or manganese) Where (B) is used in solution, its concentration is 1.2 x 10 to the power of 7-1.2 x 10 to the power of 11 counts/min(cpm), as determined by the method of Anal. Biochem., 13191983)

146, the reaction solution comprises 2-2000 ml 25 mM Hepes buffer containing 0.001-10 g treated **K5** and 10-60 mM specified cations, and reaction is at 30-40 degrees C for 1-24 hour. Where (A) is immobilized, its concentration is 1.2 x 10 to the power of 7 to 3 x 10 to the power of 11 cpm and the reaction solution is circulated through the enzyme column at 30-160 ml/hour.
Preferred Enzyme: (A) is a recombinant enzyme or is isolated from murine mastocytoma or bovine liver.

L116 ANSWER 3 OF 9 WPIX (C) 2002 THOMSON DERWENT
AN 2001-091807 [10] WPIX
DNC C2001-027154
TI Preparation of the polysaccharides K4 and **K5** from Esherichia coli comprises using an aqueous culture medium comprising defatted soya flower or the dialyzed portion of yeast autolyzate, and mineral salts and glucose .
DC A11 A96 B04 D16
IN CIPOLLETTI, G; **ORESTE, P**; PETRUCCI, F; **ZOPPETTI, G**
PA (INAL-N) INALCO SPA
CYC 94
PI WO 2001002597 A1 20010111 (200110)* EN 30p C12P019-26
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000059806 A 20010122 (200125) C12P019-26
ADT WO 2001002597 A1 WO 2000-EP6122 20000630; AU 2000059806 A AU 2000-59806 20000630
FDT AU 2000059806 A Based on WO 200102597
PRAI IT 1999-MI1465 19990702
IC ICM C12P019-26
ICS **C08B037-00**; C12N001-20
AB WO 200102597 A UPAB: 20010220
NOVELTY - Preparing the polysaccharides K4 and **K5** from Escherichia coli (E.coli) using an aqueous culture medium comprising defatted soya flower, mineral salts and glucose, or the dialyzed portion of yeast autolyzate, mineral salts and glucose, is new.
DETAILED DESCRIPTION - A new process for the preparation of the polysaccharides K4 and **K5** from Escherichia coli comprises: (a) fermentation in a submerged culture of a strain of E.coli which produces the polysaccharide K4, or of a strain of E.coli which produces the polysaccharide **K5**; (b) centrifugation of the broth culture, concentration by means of ultrafiltration of the culture filtrate, and precipitation of the polysaccharide; (c) dissolving of the precipitate and treatment with protease; and (d) passage through an ion exchange column followed by dialysis and re-precipitation; where the fermentation culture medium is composed of an aqueous mixture comprising defatted soya flower, mineral salts and glucose, or comprising the dialyzed portion of yeast autolyzate, mineral salts and glucose.
USE - For the preparation of the polysaccharides K4 and **K5** from E.coli.
ADVANTAGE - Higher yields and high purity K4 and **K5** polysaccharides are obtained with the new process, when compared with prior art.
Dwg.0/0
FS CPI
FA AB; DCN
MC CPI: A03-A; A10-G01B; B04-A10A; B04-C02F; B04-D01; B04-D02; B04-F10A3; B11-A01; D05-A04B; D05-C08; D05-H01
TECH UPTX: 20010220
TECHNOLOGY FOCUS - BIOLOGY - Preferred Process: The culture medium is

composed of an aqueous mixture comprising 0.1-5 g/l defatted soya flower or 5-30 g/l of the dialyzed portion of yeast autolyzate, 5-15 g/l K2HPO4, 0.5-5 g/l KH2PO4, 0.01-1 g/l MgCl2, 0.05-2 g/l sodium citrate, 0.1-3 g/l ammonium sulfate, and 0.5-4 g/l of glucose. The strains of E.coli used for the preparation of the polysaccharides K4 and **K5** are preferably strains O5:K4:H4 (ATCC 23502) and O10:**K5**:H4 (ATCC 23506) respectively.

ABEX

SPECIFIC COMPOUNDS - The mineral salts are composed of K2HPO4, KH2PO4, MgCl2, sodium citrate, and ammonium sulfate (claimed).
EXAMPLE - Culture medium (100 ml) preparations containing defatted soya flower (2 g/l; PROVABIS Prodotti Gianni Milan); 9.7 g/l K2HPO4, 2.0 g/l KH2PO4, 0.1 g/l MgCl2, 0.5 g/l sodium citrate, and 1.0 g/l ammonium sulfate, 2.0 g/l of glucose, in 1 liter of sterilized well water (pH 7.3) was inoculated with Escherichia coli strain O10:K5:H4 (ATCC 23506; for the preparation of K5), incubated and heat inactivated. Cells were then separated from the culture filtrate by centrifugation, and the combined culture filtrate (1 litre) was subjected to concentration by ultracentrifugation using membranes with cut-off 8,000-10,000 D down to 200 ml. During this phase a Minitan cell (Millipore) was used with flat membranes of polysulfone (PTCG). The polysaccharide K5 was precipitated by adding 4 volumes (800 ml) of 96% ethanol at 4degreesC overnight. The polysaccharide K5 has a natural tendency to sediment, thus making it possible to separate most of the supernatant liqor by siphoning. The residual precipitate was then separated by centrifugation. The precipitate was subjected to enzymatic deproteinization, using a fungal protease (Protease Type XXIII: fungal crude from Aspergillus oryzae 3.2 U/mg, code 4755, Sigma) at 4 U of protease per liter of initial culture filtrate. Following dialysis by ultracentrifugation, the precipitate was further purified by ion-exchange chromatography on a DEAE column. The fermentation yield in purified K5 was about 850 mg/l. The characteristics of K5 were then examined. For example, the assessment of molecular weight by HPLC chromatography with molecular exclusion showed that K5 consisted of 2 components of 16,000 D (70%) and PM 5,000 D (30%).

L116 ANSWER 4 OF 9 WPIX (C) 2002 THOMSON DERWENT
AN 1998-456763 [39] WPIX
DNC C1998-138053
TI Preparation of O-sulphated K4, **K5** and K40 polysaccharide(s) - with anti-angiogenesis, antiviral and anticoagulant activity.
DC B04 D21
IN CIPOLLETTI, G; **ORESTE, P; ZOPPETTI, G**
PA (INAL-N) INALCO SPA
CYC 82
PI WO 9834958 A1 19980813 (199839)* EN 20p C08B037-00 <--
RW: AT BE CH DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM GW HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
AU 9863943 A 19980826 (199902) C08B037-00 <--
EP 958307 A1 19991124 (199954) EN C08B037-00 <--
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
NZ 337399 A 20000128 (200015) C08B037-00 <--
AU 723168 B 20000817 (200044) C08B037-00 <--
IT 1289613 B 19981015 (200131) A61K000-00
JP 2001510502 W 20010731 (200148) 20p C08B037-00 <--
US 6288044 B1 20010911 (200154) A61K031-715
EP 958307 B1 20020102 (200205) EN C08B037-00 <--
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
DE 69803362 E 20020228 (200223) C08B037-00 <--
ES 2169503 T3 20020701 (200253) C08B037-00 <--

ADT WO 9834958 A1 WO 1998-EP598 19980204; AU 9863943 A AU 1998-63943 19980204; EP 958307 A1 EP 1998-909387 19980204, WO 1998-EP598 19980204; NZ 337399 A NZ 1998-337399 19980204, WO 1998-EP598 19980204; AU 723168 B AU 1998-63943 19980204; IT 1289613 B IT 1997-MI252 19970207; JP 2001510502 W JP 1998-533750 19980204, WO 1998-EP598 19980204; US 6288044 B1 WO 1998-EP598 19980204, US 1999-355211 19990723; EP 958307 B1 EP 1998-909387 19980204, WO 1998-EP598 19980204; DE 69803362 E DE 1998-603362 19980204, EP 1998-909387 19980204, WO 1998-EP598 19980204; ES 2169503 T3 EP 1998-909387 19980204

FDT AU 9863943 A Based on WO 9834958; EP 958307 A1 Based on WO 9834958; NZ 337399 A Based on WO 9834958; AU 723168 B Previous Publ. AU 9863943, Based on WO 9834958; JP 2001510502 W Based on WO 9834958; US 6288044 B1 Based on WO 9834958; EP 958307 B1 Based on WO 9834958; DE 69803362 E Based on EP 958307, Based on WO 9834958; ES 2169503 T3 Based on EP 958307

PRAI IT 1997-MI252 19970207

IC ICM A61K000-00; A61K031-715; **C08B037-00**
ICS A61K007-00; A61K007-06; A61K007-48; A61K031-125; A61K031-725; A61P031-00; A61P031-18; A61P035-00; C07H001-00

AB WO 9834958 A UPAB: 19981028
Preparation of O-sulphated K4, **K5** and K40 polysaccharides comprises: (a) suspension of K4, **K5** or K40 polysaccharide in the form of a sodium salt in an aprotic solvent; (b) O-sulphation with pyridine-sulphur trioxide or trimethylamine-sulphur trioxide adduct or with chlorosulphonic acid; (c) dilution with water or with 0.2-1N NaCl; (d) pH adjustment to a basic value; (e) precipitation by addition of EtOH saturated with NaOMe or MeOH, iPrOH or acetone; (f) dissolution by NaCl solution; (g) diafiltration; (h) precipitation of the product by EtOH; and (i) drying. Also claimed are: (1) O-sulphated K4, defructosilated K4, **K5** and K40 polysaccharides of molecular weight 4000-35000 with a sulphate/carboxy ratio of 0.5-4; and (2) O-sulphated K4, defructosilated K4, **K5** and K40 polysaccharides obtained as above where the starting K4 polysaccharide is preliminary defructosilated. Also claimed is the treatment of tumoural, HIV-1 and coagulation pathologies using 0.1-10 mg/kg/day of the compounds described in (1) above; (3) the use of the compounds described in (1) above for the preparation of pharmaceutical compositions suitable for treatment of tumoural, HIV-1 and coagulation pathologies and cosmetic compositions.

USE - The compounds have interesting anti-angiogenesis, antiviral and anticoagulant activity. The use of O-sulphated K4, defructosilated K4, **K5** and K40 polysaccharides for the preparation of compositions suitable for preventing hair loss is claimed.

Dwg.0/5

FS CPI

FA AB; DCN

MC CPI: B04-C02; B14-A02; B14-F04; B14-H01; B14-R02; D08-B03

L116 ANSWER 5 OF 9 WPIX (C) 2002 THOMSON DERWENT

AN 1998-008804 [01] WPIX

DNC C1998-003130

TI **K5** polysaccharide derivative preparation, useful as anticoagulant - by N-de acetylating **K5** polysaccharide, N-sulphating, epimerising, passing through cationic exchange resin, reacting with organic base, freeze-drying, O-sulphating etc..

DC A11 A96 B04

IN CIPOLLETTI, G; **ORESTE, P**; **ZOPPETTI, G**

PA (INAL-N) INALCO SPA

CYC 77

PI WO 9743317 A1 19971120 (199801)* EN 23p C08B037-00 <--
RW: AT BE CH DE DK EA ES FI FR GB GH GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN YU

AU 9730265 A 19971205 (199814) C08B037-00 <--
EP 897393 A1 19990224 (199912) EN C08B037-00 <--
R: AT BE CH DE DK ES FI FR GB GR IE IT LI NL PT SE
IT 1282994 B 19980403 (199952) A61K000-00
US 6162797 A 20001219 (200102) A61K031-715
EP 897393 B1 20011205 (200203) EN C08B037-00 <--
R: AT BE CH DE DK ES FI FR GB GR IE IT LI NL PT SE
DE 69708862 E 20020117 (200213) C08B037-00 <--
ES 2167748 T3 20020516 (200239) C08B037-00 <--

ADT WO 9743317 A1 WO 1997-EP2379 19970509; AU 9730265 A AU 1997-30265 19970509; EP 897393 A1 EP 1997-924941 19970509, WO 1997-EP2379 19970509; IT 1282994 B IT 1996-MI956 19960510; US 6162797 A WO 1997-EP2379 19970509, US 1998-180406 19981106; EP 897393 B1 EP 1997-924941 19970509, WO 1997-EP2379 19970509; DE 69708862 E DE 1997-608862 19970509, EP 1997-924941 19970509, WO 1997-EP2379 19970509; ES 2167748 T3 EP 1997-924941 19970509

FDT AU 9730265 A Based on WO 9743317; EP 897393 A1 Based on WO 9743317; US 6162797 A Based on WO 9743317; EP 897393 B1 Based on WO 9743317; DE 69708862 E Based on EP 897393, Based on WO 9743317; ES 2167748 T3 Based on EP 897393

PRAI IT 1996-MI956 19960510

IC ICM A61K000-00; A61K031-715; **C08B037-00**
ICS A61K031-715

AB WO 9743317 A UPAB: 19980107
Preparation of **K5** polysaccharide derivatives (I) comprises: (a) N-deacetylating a **K5** polysaccharide; (b) N-sulphating; (c) epimerising to give an iduronic acid content of at least 50% with respect to total uronic acid content; (d) dissolving the product in water and passing it through a cationic exchange resin containing column; (e) reacting with an organic base; (f) freeze-drying, redissolving the product in an organic solvent and O-sulphating; (g) precipitating, redissolving the product in distilled water and dialysing against distilled water; (h) optionally N-resulphating, and optionally depolymerising by controlled nitrous acid degradation.

Also claimed are derivatives of the **K5** polysaccharide N-deacetylated, N-sulphated, epimerised to at least 50% of iduronic acid with respect to the total of uronic acids, having: sulphate-carboxyl ratio: 2.2-2.5, N-sulphate content 70-100%, 6-O-sulphate content 70-90%, 2-O-sulphate content 50-60%, 3-O-sulphate content 5-10%, fraction having high affinity for antithrombin III 40-100%, anti-Xa 500-600 (U/mg) and APTT 250-320 (U/mg).

USE - (I) are used in anticoagulant treatment (claimed), in an amount 30-200 mg/day.

ADVANTAGE - The anti-coagulant activity is greater than that of heparin obtained by extraction from animal tissue. The method does not involve the use of large amounts of solvents and reagents employed by other methods and results in a purer final product.

Dwg.0/4

FS CPI
FA AB
MC CPI: A03-A; A10-A; A12-V01; B04-C02; B14-F04

L116 ANSWER 6 OF 9 WPIX (C) 2002 THOMSON DERWENT
AN 1996-251774 [25] WPIX
DNC C1996-079744
TI Prepn. of poly saccharide(s) with high iduronic acid content - with epimerisation stage in a buffer soln. contg. additives to give viscosity 1.1-3 centistokes.
DC B04 D16
IN CIPOLLETTI, G; **ORESTE, P**; **ZOPPETTI, G**
PA (INAL-N) INALCO SPA
CYC 68
PI WO 9614425 A1 19960517 (199625)* EN 30p C12P019-26

RW: AT BE CH DE DK ES FR GB GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG
W: AL AM AU BB BG BR BY CA CN CZ EE FI GE HU IS JP KE KG KP KR KZ LK LR LS LT LV MD MG MK MN MW MX NO NZ PL RO RU SD SG SI SK TJ TM TT UA UG US UZ VN

AU	9539261	A	19960531 (199639)		C12P019-26
EP	789777	A1	19970820 (199738)	EN	C12P019-26
	R: AT CH DE DK ES FR GB IE IT LI NL PT SE				
IT	1271057	B	19970526 (199804)		A61K000-00
JP	10508204	W	19980818 (199843)	29p	C12P019-26
US	5958899	A	19990928 (199947)		A61K031-715
EP	789777	B1	20000809 (200039)	EN	C12P019-26
	R: AT CH DE DK ES FR GB IE IT LI NL PT SE				
DE	69518333	E	20000914 (200053)		C12P019-26
ES	2150589	T3	20001201 (200105)		C12P019-26

ADT WO 9614425 A1 WO 1995-EP4241 19951030; AU 9539261 A AU 1995-39261 19951030, WO 1995-EP4241 19951030; EP 789777 A1 EP 1995-937026 19951030, WO 1995-EP4241 19951030; IT 1271057 B IT 1994-MI2240 19941104; JP 10508204 W WO 1995-EP4241 19951030, JP 1996-515019 19951030; US 5958899 A WO 1995-EP4241 19951030, US 1996-628690 19960412; EP 789777 B1 EP 1995-937026 19951030, WO 1995-EP4241 19951030; DE 69518333 E DE 1995-618333 19951030, EP 1995-937026 19951030, WO 1995-EP4241 19951030; ES 2150589 T3 EP 1995-937026 19951030

FDT AU 9539261 A Based on WO 9614425; EP 789777 A1 Based on WO 9614425; JP 10508204 W Based on WO 9614425; US 5958899 A Based on WO 9614425; EP 789777 B1 Based on WO 9614425; DE 69518333 E Based on EP 789777, Based on WO 9614425; ES 2150589 T3 Based on EP 789777

PRAI IT 1994-MI2240 19941104

REP 04Jnl.Ref; WO 9217507

IC ICM A61K000-00; A61K031-715; C12P019-26
ICS C07H005-04; **C08B037-00; C08B037-10**

ICA A61K031-725

AB WO 9614425 A UPAB: 19991122
Prepn. of polysaccharides (I) contg. > 50% L-iduronic acid (w.r.t. total uronic acids) from polysaccharide **K5** of E. coli or heparin or heparin sulphate comprises: (a) N-deacetylation of **K5** or heparin sulphate, or O-desulphation of heparan or heparin sulphate; (b) N-sulphation of the prod. of step (a); (c) at least 1 epimerisations in presence of C5 epimerase enzyme; (d) sulphation of some free OH gps. Step (c) is in a buffer soln., pH 7.4, contg. HEPES, KCl and EDTA with TRITON X-100 and one or more additives to give a viscosity of 1.1-3 centistokes. Also claimed are the polysaccharides produced as above.
USE - (I) are useful as anticoagulant and antithrombotic agents (claimed).
ADVANTAGE - The process gives yields > 50% in the epimerisation step compared to about 30% in prior art methods.
Dwg.0/0

FS CPI

FA AB

MC CPI: B04-C02; B14-F04; D05-C08; D05-H13

L116 ANSWER 7 OF 9 WPIX (C) 2002 THOMSON DERWENT

AN 1995-265453 [35] WPIX

CR 1992-326116 [40]

DNC C1995-120862

TI New N-sulphated, N-acetylated saccharide(s) - with anticoagulant and antithrombotic activity.

DC A96 B04 D16

IN CASU, B; GRAZIOLI, G; HANNESSON, H H; JANN, B; JANN, K; KUSCHE, M; LINDAHL, U; NAGGI, A; **ORESTE, P**; RAZI, N; TORRI, G; **ZOPPETTI, G**

PA (ITAF) ITALFARMACO SPA; (PLAC) MAX PLANCK GES FOERDERUNG WISSENSCHAFTEN

CYC 1

PI GB 2286193 A 19950809 (199535)* 61p C08B037-00 <--
ADT GB 2286193 A Derived from GB 1991-6757 19910328, GB 1995-8157 19950321
PRAI GB 1991-6757 19910328; GB 1995-8157 19950321
IC ICM **C08B037-00**
ICS A61K031-715; A61K031-73; A61K031-735; C12P019-04
AB GB 2286193 A UPAB: 19950918
Saccharides (I) comprising alternating uronic acid and N-sulphonated D-glucosamine residues are new. Also claimed is a modified **K5** Escherichia coli saccharide in which all the D-glucosamine units are deacetylated.
USE - (I) are anticoagulants and antithrombotic agents (I), pref having affinity for antithrombin II.
ADVANTAGE - (I) can be prepared on a larger scale than prior art prods.
Dwg.0/17
FS CPI
FA AB; DCN
MC CPI: A12-V01; B04-C02F; B14-F04; D05-C08

L116 ANSWER 8 OF 9 WPIX (C) 2002 THOMSON DERWENT
AN **1995-036410** [05] WPIX
DNC **C1995-016344**
TI Novel polysaccharide comprising repeating units of di saccharide(s) - exhibit anticoagulant and anti thrombotic activities.
DC A11 A96 B04
IN BOSSI, M L; CASU, B; GRAZIOLI, G; LINDAHL, U; NAGGI, A; **ORESTE, P** ; RAZI, N; TORRI, G
PA (ITAF) ITALFARMACO SPA
CYC 54
PI WO 9429352 A1 19941222 (199505)* EN 21p C08B037-00
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL OA PT SE
W: AT AU BB BG BR BY CA CH CN CZ DE DK ES FI GB GE HU JP KG KP KR KZ LK LU LV MD MG MN MW NL NO NZ PL PT RO RU SD SE SI SK TJ TT UA US UZ VN
AU 9468448 A 19950103 (199521) C08B037-00
ZA 9403868 A 19950426 (199522) 21p C08B000-00
IT 1270823 B 19970513 (199803) C08B000-00
ADT WO 9429352 A1 WO 1994-EP1660 19940524; AU 9468448 A AU 1994-68448 19940524; ZA 9403868 A ZA 1994-3868 19940602; IT 1270823 B IT 1993-MI1175 19930604
FDT AU 9468448 A Based on WO 9429352
PRAI IT 1993-MI1175 19930604
REP 01Jnl.Ref; EP 209924; EP 544592; WO 9217507
IC A61K031-725; C08B037-10
AB WO 9429352 A UPAB: 19951204
Polysaccharides consisting of repeating disaccharide structures of formula (I) or their alkali or alkaline earth metal salts comprise chains or mixts. of chains having a mol.wt. of 1000-greater than100,000 Da. A = D-glucuronic acid moiety; B = D-glucosamine moiety; R = H, acetyl or sulphate (at least 20% being sulphate and the remaining mainly acetyl); R1-R4 = H or sulphate (at least one of R,R1 and R2 being sulphate and R3 and R4 being H).
USE - The polysaccharides exhibit anticoagulant and antithrombic properties.
ADVANTAGE - The polysaccharides have better activity than structurally related cpds. disclosed in EP-489647 and WO9217507.
Dwg.0/3
FS CPI
FA AB; GI; DCN
MC CPI: A03-A00A; A09-A; A12-V01; B04-C02; B14-F08

L116 ANSWER 9 OF 9 WPIX (C) 2002 THOMSON DERWENT
AN 1992-326116 [40] WPIX

CR 1995-265453 [35]
DNC C1992-144827
TI New N-de acetylated derivs. of **K-5** E. Coli saccharide - contain at least 35 per cent N-sulphate gps. and may also be C5 epimerised or O-sulphated, useful as anticoagulants and antithrombotic agents.
DC A11 A96 B04 D16
IN CASU, B; GRAZIOLI, G; HANNESSON, H H; JANN, B; JANN, K; KUSCHE, M; LINDAHL, U; NAGGI, A; **ORESTE, P**; RAZI, N; TORRI, G; **ZOPPETTI, G**; HANNESSON, H; TORR, G
PA (ITAF) ITALFARMACO SPA; (PLAC) MAX PLANCK GES FOERDERUNG WISS; (TUBB-I) TUBBY D G; (ITAF) ITAL-FARMACO SPA; (PLAC) MAX PLANCK GES FOERDERUNG WISSENSCHAFTEN; (PLAC) MAX PLANCK INST IMMUNOBIOLOGIE; (MAXP-N) MAX PLANCK INST IMMUNOBIOLOGIE; (MAXP-N) PLANCK INST IMMUNBIOLOGIE MAX
CYC 41
PI GB 2254083 A 19920930 (199240)* 57p C08B037-00 <--
WO 9217507 A1 19921015 (199244) EN 81p C08B037-00 <--
RW: AT BE CH DE DK ES FR GB GR IT LU MC NL OA SE
W: AT AU BB BG BR CA CH CS DE DK ES FI GB HU JP KP KR LK LU MG MN MW NL NO PL RO RU SD SE US
AU 9214308 A 19921102 (199305) C08B037-00 <--
PT 100316 A 19930730 (199334) C12P019-00
TW 209225 A 19930711 (199343) C07H001-00
ZA 9202313 A 19931027 (199348) 79p C08B000-00 <--
FI 9304141 A 19930922 (199349) C08B000-00 <--
EP 577665 A1 19940112 (199402) EN C08B037-00 <--
R: AT BE CH DE DK ES FR GB GR IT LI LU MC NL SE
NO 9303440 A 19931026 (199403) C08B037-00 <--
NZ 242163 A 19940526 (199424) C08B037-10 <--
HU 67208 T 19950228 (199514) C08B037-00 <--
JP 07501684 W 19950223 (199517) C12P019-26
IT 1254564 B 19950925 (199614) C08B000-00 <--
ADT GB 2254083 A GB 1991-6757 19910328; WO 9217507 A1 WO 1992-GB571 19920330; AU 9214308 A AU 1992-14308 19920330, WO 1992-GB571 19920330; PT 100316 A PT 1992-100316 19920327; TW 209225 A TW 1992-103646 19920511; ZA 9202313 A ZA 1992-2313 19920330; FI 9304141 A WO 1992-GB571 19920330, FI 1993-4141 19930922; EP 577665 A1 EP 1992-907206 19920330, WO 1992-GB571 19920330; NO 9303440 A WO 1992-GB571 19920330, NO 1993-3440 19930927; NZ 242163 A NZ 1992-242163 19920330; HU 67208 T WO 1992-GB571 19920330, HU 1993-2732 19920330; JP 07501684 W JP 1992-506945 19920330, WO 1992-GB571 19920330; IT 1254564 B IT 1992-MI722 19920326
FDT AU 9214308 A Based on WO 9217507; EP 577665 A1 Based on WO 9217507; HU 67208 T Based on WO 9217507; JP 07501684 W Based on WO 9217507
PRAI GB 1991-6757 19910328
REP 2.Jnl.Ref; EP 340628; EP 489647
IC ICM C07H001-00; **C08B000-00**; **C08B037-00**; **C08B037-10**; C12P019-00; C12P019-26
ICS A61K031-70; A61K031-715; A61K031-73; A61K031-735; A61K035-74; C07H015-04; C12N001-20; C12P019-04; C12P019-24
ICA A61K031-725
AB GB 2254083 A UPAB: 19960308
Deacetylated **K-5** E. coli saccharide, where the deacetylation amts. to at least 35% of the acetyl gps. of naturally occurring **K-5**, is claimed.

Sulphate gps. may be substd. in all of the positions on **K-5** which have been deacetylated, these positions may be the amine gps. of the glucosamine residues. At least some of the glucuronic acid residues may be epimerised to L-iduronic acid residues. At least some of the free OH gps. of the saccharide may be sulphated.

USE/ADVANTAGE - The polysaccharide prods. can be obtd. in large amts. and have high antithrombotic and anticoagulant activ

Dwg.0/17
Dwg.0/17

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FS   CPI
FA   AB; DCN
ABEQ ZA   9202313 A UPAB: 19940120
     The present invention relates to anticoagulants prepd. from the K5
     saccharide of E. coli which have good activity and can be mass produced.


=> d his

     (FILE 'HOME' ENTERED AT 13:57:56 ON 07 DEC 2002)
               SET COST OFF

     FILE 'REGISTRY' ENTERED AT 13:58:07 ON 07 DEC 2002
               E K5/CN
L1           1 S E4

     FILE 'HCAPLUS' ENTERED AT 13:58:49 ON 07 DEC 2002
               E ORESTE P/AU
L2          32 S E3-E5
               E ZOPPETTI G/AU
L3          46 S E3,E4
L4          23 S L2 AND L3
L5          13 S L2,L3 AND K5(L)?SACCHARID?
               E IT2000-MI665/AP,PRN
L6           2 S E3,E4
L7           2 S L6 AND L2-L6
L8          11 S L5 NOT L7
L9          13 S L2,L3 AND CARBOHYDRATE?/SC,SX,CW
L10          5 S L9 NOT L5-L8
               SEL DN AN 2 5
L11          2 S L10 AND E1-E6
L12         15 S L7,L8,L11 AND L2-L11
               SEL RN

     FILE 'REGISTRY' ENTERED AT 14:03:17 ON 07 DEC 2002
L13         54 S E7-E60
L14          8 S L13 AND OC5/ES
L15         10 S L13 AND (N AND S)/ELS
L16          6 S L15 AND L14
L17          6 S L14,L15 NOT L16
L18            STR
L19         11 S L18
               E K 5/CN
L20          1 S E11
L21        373 S L18 FUL
               SAV L21 KRISH950/A

     FILE 'HCAPLUS' ENTERED AT 14:09:25 ON 07 DEC 2002
L22          7 S L20
L23        129 S (K5 OR K 5)(L)?SACCHARID?
L24        129 S L22,L23
L25        279 S L21
L26          3 S L24 AND L25
L27         13 S L2,L3 AND L24
L28          2 S L2,L3 AND L25
L29          3 S L26,L28
L30          5 S L7,L29
L31         16 S L12,L26-L30
L32          3 S L25 AND L31
L33         16 S L31,L32

     FILE 'REGISTRY' ENTERED AT 14:15:08 ON 07 DEC 2002
L34       1043 S ?EPIMERASE?/CNS
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     FILE 'HCAPLUS' ENTERED AT 14:15:20 ON 07 DEC 2002
L35        1984 S L34
L36        2049 S ?EPIMERASE?
L37        2585 S L35,L36
L38           9 S L37 AND L24
L39           1 S L37 AND L25
L40          22 S L33,L38,L39
L41       11238 S ?EPIMERI?
L42          13 S L41 AND L24
L43           1 S L41 AND L25
L44          27 S L40,L42,L43
L45           0 S L44 AND EPIMERIS?
L46          13 S L44 AND EPIMERIZ?
L47          27 S L44,L46
L48          43 S L24,L25 AND (GLUCURON? AND IDURON?)

     FILE 'REGISTRY' ENTERED AT 14:19:38 ON 07 DEC 2002
L49           1 S DIMETHYL SULFOXIDE/CN
L50           1 S METHANOL/CN
                E BARIUM, ION/CN
L51           1 S E19
                E CALCIUM, ION/CN
L52           1 S E23
                E MAGNESIUM, ION/CN
L53           1 S E17
                E MANGANESE, ION/CN
L54           1 S E20
                E BARIUM CHLORIDE/CN
L55           1 S E3
                E CALCIUM CHLORIDE/CN
L56           1 S E3
                E MAGNESIUM CHLORIDE/CN
L57           1 S E3
                E MANGANESE CHLORIDE/CN
L58           2 S E3
                E PYRIDINE SULFUR TRIOXIDE/CN
L59           1 S E3
                E TRIMETHYLAMINE SULFUR TRIOXIDE/CN
L60           1 S E3
L61           1 S E4
                E SODIUM BOROHYDRIDE/CN
L62           1 S E3
L63          46 S L13 NOT OC5/ES
L64          23 S L63 NOT UNSPECIFIED
L65          12 S L64 NOT L49-L62
L66           1 S L65 AND NITROUS ACID/CN
L67           2 S L65 AND NC5/ES
L68           3 S L65 AND O3S
L69           7 S L65 NOT L66-L68

     FILE 'HCAPLUS' ENTERED AT 14:28:08 ON 07 DEC 2002
L70       52343 S L49 OR DMSO OR DIMETHYLSULFOXIDE OR DIMETHYLSULPHOXIDE OR (DI
L71      419479 S L50 OR MEOH OR METHANOL OR METHYLALCOHOL OR METHYL ALCOHOL
L72           1 S L24,L25 AND L70 AND L71
L73           2 S L24,L25 AND L51-L58
L74          16 S L24,L25 AND (DIVALENT(L)CATION OR BARIUM OR CALCIUM OR MAGNES
L75           1 S L24,L25 AND (L62 OR (NA OR SODIUM)()BOROHYDRIDE)
L76           8 S L24,L25 AND L59-L61,L66-L68
L77          43 S L72-L76,L47
L78           8 S L48 AND L77
L79          30 S L72,L73,L75,L76,L78,L47
L80          23 S L24,L25 AND SULFAT?/CW
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L81           7 S L24,L25 AND DEACET?/CW
L82          13 S L79 AND L80,L81
L83          40 S L79-L82
L84          14 S L83 AND ?GLYCOSAMINOGLYCAN?
L85          27 S L83 AND L24
L86          27 S L83 AND L47
L87           5 S L83 NOT L84-L86
L88        4995 S ANTITHROMBIN III
L89        4475 S FACTOR XA
L90        5715 S FACTOR II

     FILE 'REGISTRY' ENTERED AT 14:37:49 ON 07 DEC 2002
L91           3 S 9000-94-6 OR 9002-04-4 OR 9002-05-5
                E FACTOR II/CN
L92           1 S E3 NOT CO/ELS

     FILE 'HCAPLUS' ENTERED AT 14:38:59 ON 07 DEC 2002
L93       22987 S L91,L92
L94           9 S L83 AND L88-L90,L93
L95          28 S L86,L94
L96          12 S L83 NOT L95
L97          40 S L2,L3 NOT L95,L96
                SEL DN AN 1
L98           1 S L97 AND E1-E3
L99          29 S L98,L95 AND L2-L12,L22-L33,L35-L48,L70-L90,L93-L98
L100         12 S L83 NOT L99
                SEL DN AN 3 5
L101          2 S L100 AND E4-E9
L102         31 S L99,L101
                SEL HIT RN

     FILE 'REGISTRY' ENTERED AT 14:44:29 ON 07 DEC 2002
L103         48 S E10-E57
L104         25 S L103 AND L21
L105         23 S L103 NOT L104
L106          1 S L105 AND K 5
L107         22 S L105 NOT L106

     FILE 'REGISTRY' ENTERED AT 14:46:04 ON 07 DEC 2002

     FILE 'HCAPLUS' ENTERED AT 14:46:34 ON 07 DEC 2002

     FILE 'WPIX' ENTERED AT 14:47:09 ON 07 DEC 2002
                E ORESTE P/AU
L108         13 S E3
                E ZOPPETTI G/AU
L109         14 S E3
L110         15 S L108,L109
L111         12 S L110 AND C08B/IC,ICM,ICS
L112          8 S L110 AND (K5 OR K 5)
L113          8 S L111 AND L112
L114          7 S L110 NOT L113
                SEL DN AN 4
L115          1 S E1-E2 AND L114
L116          9 S L113,L115

     FILE 'WPIX' ENTERED AT 14:49:06 ON 07 DEC 2002
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STN search from related case # 09/738879.

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 NEWS  4  Apr 09   ZDB will be removed from STN
 NEWS  5  Apr 19   US Patent Applications available in IFICDB, IFIPAT, and IFIUDB
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 NEWS 11  Jun 10   PCTFULL has been reloaded
 NEWS 12  Jul 02   FOREGE no longer contains STANDARDS file segment
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                   saved answer sets no longer valid
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 NEWS 16  Aug 08   CANCERLIT reload
 NEWS 17  Aug 08   PHARMAMarketLetter(PHARMAML) - new on STN
 NEWS 18  Aug 08   NTIS has been reloaded and enhanced
 NEWS 19  Aug 19   Aquatic Toxicity Information Retrieval (AQUIRE)
                   now available on STN
 NEWS 20  Aug 19   IFIPAT, IFICDB, and IFIUDB have been reloaded
 NEWS 21  Aug 19   The MEDLINE file segment of TOXCENTER has been reloaded
 NEWS 22  Aug 26   Sequence searching in REGISTRY enhanced
 NEWS 23  Sep 03   JAPIO has been reloaded and enhanced
 NEWS 24  Sep 16   Experimental properties added to the REGISTRY file
 NEWS 25  Sep 16   Indexing added to some pre-1967 records in CA/CAPLUS
 NEWS 26  Sep 16   CA Section Thesaurus available in CAPLUS and CA

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